	L #	Hits	Search Text	DBs	Time Stamp
1	L3	14987	biolumines$ or fluorescen$ near4 protein$1 or luciferase$1 or photoprotein$1	USPAT; US-PGPUB	2003/02/24 15:09
2	L4	134615	bubble$	USPAT; US-PGPUB	2003/02/24 15:10
3	L5	878	3 and 4	USPAT; US-PGPUB	2003/02/24 15:10
4	L6	15	3 same 4	USPAT; US-PGPUB	2003/02/24 15:11
5	L7	68310	toy or novelty	USPAT; US-PGPUB	2003/02/24 15:40
6	L8	30	5 and 7	USPAT; US-PGPUB	2003/02/24 15:40

PGPUB-DOCUMENT-NUMBER: 20020164663

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020164663 A1

TITLE: Methods and compositions for detection, diagnosis and prediction of antiestrogen-resistant breast cancer

PUBLICATION-DATE: November 7, 2002

US-CL-CURRENT: 435/7.23

APPL-NO: 09/ 877794

DATE FILED: June 8, 2001

RELATED-US-APPL-DATA:

child 09877794 A1 20010608 parent continuation-of PCT/US99/28206 19991129 US UNKNOWN non-provisional-of-provisional 60111428 19981208 US

PGPUB-DOCUMENT-NUMBER: 20020004942

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020004942 A1

TITLE: Bioluminescent novelty items

PUBLICATION-DATE: January 10, 2002

US-CL-CURRENT: 800/288

APPL-NO: 09/ 803211

DATE FILED: March 8, 2001

RELATED-US-APPL-DATA:

child 09803211 A1 20010308 parent continuation-of 09444762 19991122 US PENDING
child 09444762 19991122 US parent continuation-of 09135988 19980817 US GRANTED
parent-patent 6152358 US child 09444762 19991122 US parent continuation-of
08757046 19961125 US GRANTED parent-patent 5876995 US child 09444762 19991122
US parent continuation-of 08597274 19960206 US GRANTED parent-patent 6247995 US
non-provisional-of-provisional 60079624 19980327 US
non-provisional-of-provisional 60089367 19980615 US

RELATED APPLICATIONS

[0001] This application is a continuation of U.S. application Ser. No. 09/444,762 to Bruce Bryan, filed Nov. 22, 1999, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also continuation of U.S. application Ser. No. 09/135,988 to Bruce Bryan, filed Aug. 17, 1998, now U.S. Pat. No. 6,152,358, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also continuation-in-part of U.S. application Ser. No. 08/757,046 to Bruce Bryan, filed Nov. 25, 1996, now U.S. Pat. No. 5,876,995, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also a continuation-in-part of U.S. application Ser. No. 08/597,274, now allowed, to Bruce Bryan, filed Feb. 6, 1996, entitled "BIOLUMINESCENT NOVELTY ITEMS". [0002] U.S. application Ser. No. 09/444,762 is a continuation of U.S. application Ser. No. 09/135,988, which is a continuation-in-part of U.S. application Ser. No. 08/757,046, which is a continuation-in-part of U.S. application Ser. No. 08/597,274. The subject matter of each of U.S. application Ser. Nos. 09/135,988, 08/597,274 and 08/757,046 is herein incorporated in its entirety by reference thereto. This application is also related to provisional application Ser. Nos. 60/079,624 and 60/089,367. The disclosures of each of the above noted patents, applications and provisional applications is incorporated herein by reference thereto.

PGPUB-DOCUMENT-NUMBER: 20010010367

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010010367 A1

TITLE: Luminescent gel coats and moldable resins

PUBLICATION-DATE: August 2, 2001

US-CL-CURRENT: 252/301.36

APPL-NO: 09/ 766415

DATE FILED: January 18, 2001

RELATED-US-APPL-DATA:

child 09766415 A1 20010118 parent division-of 09170432 19981013 US GRANTED
parent-patent 6207077 US

US-PAT-NO: 6462038
DOCUMENT-IDENTIFIER: US 6462038 B1

TITLE: Androgen receptor modulator compounds and methods

DATE-ISSUED: October 8, 2002

US-CL-CURRENT: 514/224.5; 514/229.8 ; 514/250 ; 514/291 ; 544/101 ; 544/34 ; 544/345 ; 546/80 ; 546/89 ; 546/90

APPL-NO: 09/ 648684

DATE FILED: August 25, 2000

PARENT-CASE:

This application claims priority to U.S. Provisional Application Ser. No. 60/150,988, filed Aug. 27, 1999, the entire disclosure of which is incorporated by reference herein.

US-PAT-NO: 6458547
DOCUMENT-IDENTIFIER: US 6458547 B1

TITLE: Apparatus and method for detecting and identifying infectious agents

DATE-ISSUED: October 1, 2002

US-CL-CURRENT: 435/7.1; 356/215 ; 356/222 ; 356/317 ; 422/57 ; 422/58 ; 422/82.05 ; 422/82.08 ; 435/288.7 ; 435/6 ; 435/808 ; 435/973 ; 435/975 ; 436/172 ; 436/527 ; 436/805

APPL-NO: 08/ 990103

DATE FILED: December 12, 1997

PARENT-CASE:

RELATED APPLICATIONS This application claims priority under 35 U.S.C. .sctn.119(e) to U.S. Provisional appplication Ser. No. 60/037,675, filed Feb. 11, 1997 and to U.S. Provisional application Ser. No. 60/033,745, filed Dec. 12, 1996.

US-PAT-NO: 6448405
DOCUMENT-IDENTIFIER: US 6448405 B1

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: September 10, 2002

US-CL-CURRENT: 546/62; 549/390

APPL-NO: 08/ 947428

DATE FILED: October 8, 1997

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is divisional of 08,465,429, filed on Jun. 5, 1995, U.S. Pat. No. 5,696,127, which is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994, now abandoned the entire disclosure of which is herein incorporated by reference.

US-PAT-NO: 6436682
DOCUMENT-IDENTIFIER: US 6436682 B1

TITLE: Luciferases, fluorescent proteins, nucleic acids encoding the luciferases and fluorescent proteins and the use thereof in diagnostics, high throughput screening and novelty items

DATE-ISSUED: August 20, 2002

US-CL-CURRENT: 435/189; 124/74 ; 124/76 ; 222/1 ; 42/54 ; 435/183 ; 446/473

APPL-NO: 09/ 609161

DATE FILED: June 30, 2000

PARENT-CASE:

RELATED APPLICATIONS This application is a divisional of U.S. application Ser. No. 09/277,716, filed Mar. 26, 1999 to Bruce Bryan and Christopher Szent-Gyorgyi, entitled "LUCIFERASES, FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE LUCIFERASES AND FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS." Now U.S. Pat. No. 6,232,107, filed May 15, 2001. This application also claims priority to U.S. provisional application Ser. No. 60/102,939, filed Oct. 1, 1998, to Bruce Bryan and Christopher Szent-Gyorgyi, entitled "LUCIFERASES, FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE LUCIFERASES AND FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS". Priority is also claimed to U.S. provisional application Serial No. 60/089,367, filed Jun. 15, 1998, to Bruce Bryan and Christopher Szent-Gyorgyi, entitled "GAUSSIA LUCIFERASE, NUCLEIC ACIDS ENCODING THE LUCIFERASE AND METHODS USING THE LUCIFERASE", and to U.S. provisional application Serial No. 60/079,624, filed Mar. 27, 1998, to Bruce Bryan and Christopher Szent-Gyorgyi, entitled "RENILLA GREEN FLUORESCENT PROTEIN COMPOSITIONS AND METHODS " Benefit of priority to each of these applications is claimed under 35 U.S.C. .sctn.119(e). This application is also related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS", now U.S. Pat. No. 5,876,995, issued Mar. 2, 1999, and in U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1 997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASTIC TISSUE AND OTHER TISSUES". The application is also related to U.S. application Ser. No. 08/990,103, filed Dec. 12, 1997, to Bruce Bryan entitled "APPARATUS AND

of each of the above noted U.S. applications and provisional applications is herein incorporated by reference in its entirety.

US-PAT-NO: 6247995
DOCUMENT-IDENTIFIER: US 6247995 B1

TITLE: Bioluminescent novelty items

DATE-ISSUED: June 19, 2001

US-CL-CURRENT: 446/473; 124/74 ; 124/76 ; 222/1 ; 42/54 ; 435/189

APPL-NO: 08/ 597274

DATE FILED: February 6, 1996

US-PAT-NO: 6232107
DOCUMENT-IDENTIFIER: US 6232107 B1

TITLE: Luciferases, fluorescent proteins, nucleic acids encoding the luciferases and fluorescent proteins and the use thereof in diagnostics, high throughput screening and novelty items

DATE-ISSUED: May 15, 2001

US-CL-CURRENT: 435/189; 435/183 ; 435/252.2 ; 435/320.1 ; 435/6 ; 435/69.1 ; 435/8

APPL-NO: 09/ 277716

DATE FILED: March 26, 1999

PARENT CASE:

RELATED APPLICATIONS This application claims priority to U.S. provisional application Ser. No. 60/102,939, filed Oct. 1, 1998, to Bruce Bryan and Christopher Szent-Gyorgyi, entitled "LUCIFERASES, FLUORESCENT PROTEINS, NUCLEIC ACIDS ENCODING THE LUCIFERASES AND FLUORESCENT PROTEINS AND THE USE THEREOF IN DIAGNOSTICS, HIGH THROUGHPUT SCREENING AND NOVELTY ITEMS". Priority is also claimed to U.S. provisional application Ser. No.60/089,367, filed Jun. 15, 1998, to Bruce Bryan and Christopher Szent-Gyorgyi, entitled "GAUSSIA LUCIFERASE, NUCLEIC ACIDS ENCODING THE LUCIFERASE AND METHODS USING THE LUCIFERASE", and to U.S. provisional application Ser. No.60/079,624, filed Mar. 27, 1998, to Bruce Bryan and Christopher Szent-Gyorgyi, entitled "RENILLA GREEN FLUORESCENT PROTEIN COMPOSITIONS AND METHODS." For U.S. purposes, benefit of priority to each of these applications is claimed under 35 U.S.C. .sctn.119(e). This application is also related to subject matter in U.S. application Ser. No. 08/757,046, filed Nov. 25, 1996, to Bruce Bryan entitled "BIOLUMINESCENT NOVELTY ITEMS", now U.S. Pat. No. 5,876,995, issued Mar. 2, 1999, and in U.S. application Ser. No. 08/597,274, filed Feb. 6, 1996, to Bruce Bryan, entitled "BIOLUMINESCENT NOVELTY ITEMS". This application is also related to U.S. application Ser. No. 08/908,909, filed Aug. 8, 1997, to Bruce Bryan entitled "DETECTION AND VISUALIZATION OF NEOPLASTIC TISSUE AND OTHER TISSUES". The application is also related to U.S. application Ser. No. 08/990,103, filed Dec. 12, 1997, to Bruce Bryan entitled "APPARATUS AND METHODS FOR DETECTING AND IDENTIFYING INFECTIOUS AGENTS". The subject matter of each of the above noted U.S. applications and provisional applications is herein incorporated by reference in its entirety.

US-PAT-NO: 6207077
DOCUMENT-IDENTIFIER: US 6207077 B1

TITLE: Luminescent gel coats and moldable resins

DATE-ISSUED: March 27, 2001

US-CL-CURRENT: 252/301.36; 428/690 ; 523/514 ; 523/521 ; 523/526 ; 524/403 ; 524/418 ; 524/420 ; 524/423 ; 524/427 ; 524/437 ; 524/442 ; 524/449 ; 524/783 ; 524/786 ; 524/787 ; 525/12 ; 525/15 ; 525/23

APPL-NO: 09/ 170432

DATE FILED: October 13, 1998

US-PAT-NO: 6152358
DOCUMENT-IDENTIFIER: US 6152358 A

TITLE: Bioluminescent novelty items

DATE-ISSUED: November 28, 2000

US-CL-CURRENT: 229/87.19; 435/189 ; 493/955

APPL-NO: 09/ 135988

DATE FILED: August 17, 1998

PARENT-CASE:

RELATED APPLICATIONS This application is a continuation-in-part of U.S. application Ser. No. 08/757,046 to Bruce Bryan, filed Nov. 25, 1996, entitled "BIOLUMINESCENT NOVELTY ITEMS,"now U.S. Pat. No. 5,876,995. This application is also a continuation-in-part of U.S. application Ser. No. 08/597,274 to Bruce Bryan, filed Feb. 6, 1996, entitled "BIOLUMINESCENT NOVELTY ITEMS". U.S. application Ser. No. 08/757,046 is a continuation-in-part of U.S. application Ser. No. 08/597,274. The subject matter of each of U.S. application Ser. No. 08/597,274 and U.S. application Ser. No. 08/757,046 is herein incorporated in its entirety by reference thereto. The disclosures of each of the above noted applications and provisional application is incorporated herein by reference thereto.

US-PAT-NO: 6121450
DOCUMENT-IDENTIFIER: US 6121450 A

TITLE: Intermediates for preparation of steroid receptor modulator compounds

DATE-ISSUED: September 19, 2000

US-CL-CURRENT: 546/81

APPL-NO: 08/ 947427

DATE FILED: October 8, 1997

PARENT-CASE:

RELATED PATENT APPLICATIONS This is a divisional of copending application Ser. No. 08/462,643, filed on Jun. 5, 1995, which is in turn a Continuation-In-Part of Ser. No. 08/363,529, filed Dec. 22, 1994 now abandoned.

US-PAT-NO: 6113886
DOCUMENT-IDENTIFIER: US 6113886 A

TITLE: Bioluminescent novelty items

DATE-ISSUED: September 5, 2000

US-CL-CURRENT: 424/49; 424/63 ; 424/64 ; 424/69 ; 424/70.1 ; 424/70.6 ; 424/70.7 ; 424/78.02 ; 424/94.4 ; 435/189 ; 510/119 ; 510/135 ; 510/392 ; 510/481

APPL-NO: 09/ 447208

DATE FILED: November 22, 1999

PARENT-CASE:

RELATED APPLICATIONS This application is a divisional of U.S. application Ser. No. 09/135,988 to Bruce Bryan, filed Aug. 17, 1998, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also continuation-in-part of U.S. application Ser. No. 08/757,046, now U.S. Pat. No. 5,876,995, to Bruce Bryan, filed Nov. 25, 1996, entitled "BIOLUMINESCENT NOVELTY ITEMS." This application is also a continuation-in-part of U.S. application Ser. No. 08/597,274, now allowed, to Bruce Bryan, filed Feb. 6, 1996, entitled "BIOLUMINESCENT NOVELTY ITEMS". U.S. Pat. No. 09/135,988 is a continuation-in-part of U.S. application Ser. No. 08/757,046, which is a continuation-in-part of U.S. application Ser. No. 08/597,274. The subject matter of each of U.S. application Ser. Nos. 09/135,988, 08/597,274 and 08/757,046 is herein incorporated in its entirety by reference thereto. This application is also related to provisional application Ser. Nos. 60/079,624 and 60/089,367. The disclosures of each of the above noted applications and provisional applications is incorporated herein by reference thereto.

US-PAT-NO: 6093821
DOCUMENT-IDENTIFIER: US 6093821 A

TITLE: Process for preparing steroid receptor modulator compounds

DATE-ISSUED: July 25, 2000

US-CL-CURRENT: 544/333; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/249 ; 544/284 ; 544/338 ; 544/342 ; 544/344 ; 544/353 ; 546/152 ; 546/153 ; 546/159 ; 546/165 ; 546/167 ; 546/168 ; 546/173 ; 546/178 ; 546/179 ; 546/180

APPL-NO: 08/ 943853

DATE FILED: October 8, 1997

PARENT-CASE:

RELATED PATENT APPLICATIONS This is a divisional of application(s) Ser. No. 08/464,541, filed on Jun. 5, 1995 U.S. Pat. No. 5,688,810, which is in turn a Continuation-In-Part of Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned.

US-PAT-NO: 5994544
DOCUMENT-IDENTIFIER: US 5994544 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: November 30, 1999

US-CL-CURRENT: 546/62; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/342 ; 544/343 ; 544/344 ; 544/353 ; 544/383

APPL-NO: 08/ 947413

DATE FILED: October 8, 1997

PARENT-CASE:

RELATED PATENT APPLICATIONS This is a divisional of application Ser. No. 08/464,360, filed on Jun. 5, 1995, U.S. Pat. No. 5,693,646, which is in turn a Continuation-In-Part of Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned.

US-PAT-NO: 5879894
DOCUMENT-IDENTIFIER: US 5879894 A

TITLE: Long emission wavelength chemiluminescent compounds and their use in test assays

DATE-ISSUED: March 9, 1999

US-CL-CURRENT: 435/7.1; 436/172 ; 436/501 ; 436/536

APPL-NO: 08/ 308772

DATE FILED: September 19, 1994

PARENT-CASE:

This is a continuation-in-part application of application Ser. No. 08/035,130, filed on Mar. 19, 1993, now U.S. Pat. No. 5,395,752.

US-PAT-NO: 5876995
DOCUMENT-IDENTIFIER: US 5876995 A

TITLE: Bioluminescent novelty items

DATE-ISSUED: March 2, 1999

US-CL-CURRENT: 435/189; 426/104 ; 426/250 ; 426/262 ; 426/268 ; 426/383 ; 426/422 ; 426/540 ; 426/590 ; 426/592 ; 426/656 ; 426/66 ; 530/350

APPL-NO: 08/ 757046

DATE FILED: November 25, 1996

PARENT-CASE:

RELATED APPLICATIONS This application is a continuation in part of U.S. application Ser. No. 08/597,274 to Bruce Bryan, filed Feb. 6, 1996, entitled "BIOLUMINESCENT NOVELTY ITEMS". The subject matter of U.S. application Ser. No. 08/597,274 is herein incorporated in its entirety by reference thereto.

US-PAT-NO: 5780239
DOCUMENT-IDENTIFIER: US 5780239 A

TITLE: Method for the determination of cast in urine

DATE-ISSUED: July 14, 1998

US-CL-CURRENT: 435/7.1; 435/7.9 ; 436/518 ; 436/87

APPL-NO: 08/ 675386

DATE FILED: July 2, 1996

PARENT-CASE:

PRIOR APPLICATIONS This application is a continuation in part of application Ser. No. 08/347,124, filed Nov. 23, 1994, now abandoned

US-PAT-NO: 5770383
DOCUMENT-IDENTIFIER: US 5770383 A

TITLE: Tricyclic retinoids, methods for their production and use

DATE-ISSUED: June 23, 1998

US-CL-CURRENT: 435/7.1; 514/217 ; 514/290 ; 514/454 ; 514/510 ; 514/569 ; 530/350 ; 530/369 ; 530/412 ; 540/586 ; 546/101 ; 549/388 ; 560/8 ; 562/405

APPL-NO: 08/ 475397

DATE FILED: June 7, 1995

PARENT-CASE:

REFERENCE TO RELATED APPLICATIONS This application is a Continuation-In-Part application of U.S. patent application Ser. No. 08/366,630, filed Dec. 30, 1994, now abandoned, the entire disclosure of which is herein incorporated by reference.

US-PAT-NO: 5770382
DOCUMENT-IDENTIFIER: US 5770382 A

TITLE: Tricyclic retinoids, methods for their production and use

DATE-ISSUED: June 23, 1998

US-CL-CURRENT: 435/7.1; 514/217 ; 514/290 ; 514/454 ; 514/510 ; 514/569 ; 530/350 ; 530/369 ; 530/412 ; 540/586 ; 546/101 ; 549/388 ; 560/8 ; 562/405

APPL-NO: 08/ 475514

DATE FILED: June 7, 1995

PARENT-CASE:

REFERENCE TO RELATED APPLICATIONS This application is a Continuation-In-Part application of U.S. Pat. application Ser. No. 08/366,630, filed Dec. 30, 1994, now abandoned, the entire disclosure of which is herein incorporated by reference.

US-PAT-NO: 5770378
DOCUMENT-IDENTIFIER: US 5770378 A

TITLE: Tricyclic retinoids, methods for their production and use

DATE-ISSUED: June 23, 1998

US-CL-CURRENT: 435/7.1; 514/217 ; 514/290 ; 514/454 ; 514/510 ; 514/569 ; 530/350 ; 530/369 ; 530/412 ; 540/586 ; 546/101 ; 549/388 ; 560/8 ; 562/405

APPL-NO: 08/ 472127

DATE FILED: June 7, 1995

PARENT-CASE:

REFERENCE TO RELATED APPLICATIONS This Application is a Continuation In Part application of U.S. Pat. application Ser. No. 08/366,630, filed Nov. 30, 1994, now abandoned, the entire disclosure of which is herein incorporated by reference.

US-PAT-NO: 5702887
DOCUMENT-IDENTIFIER: US 5702887 A

TITLE: Long emission wavelength chemiluminescent compounds and their use in test assays

DATE-ISSUED: December 30, 1997

US-CL-CURRENT: 435/6; 252/700 ; 435/7.1 ; 436/501 ; 546/71

APPL-NO: 08/ 340093

DATE FILED: November 14, 1994

PARENT-CASE:

This is a divisional of application Ser. No. 08/035,130 filed on Mar. 19, 1993, U.S. Pat. No. 5,395,752.

US-PAT-NO: 5696133
DOCUMENT-IDENTIFIER: US 5696133 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: December 9, 1997

US-CL-CURRENT: 514/314; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/252.04 ; 514/253.06 ; 514/253.07 ; 514/256 ; 514/267 ; 514/291 ; 514/292 ; 514/311 ; 514/312

APPL-NO: 08/ 465556

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 23, 1994 abandoned, the entire disclosure of which is herein incorporated by reference.

US-PAT-NO: 5696130
DOCUMENT-IDENTIFIER: US 5696130 A

TITLE: Tricyclic steroid receptor modulator compounds and methods

DATE-ISSUED: December 9, 1997

US-CL-CURRENT: 514/291; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/252.04 ; 514/253.03 ; 514/255.05 ; 514/256 ; 514/292 ; 514/411 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/338 ; 544/342 ; 544/343 ; 544/344 ; 544/353 ; 546/81 ; 546/84 ; 546/89 ; 546/92 ; 548/432

APPL-NO: 08/ 462643

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of United States patent application Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned, the entire disclosure of which is herein incorporated by reference.

US-PAT-NO: 5696127
DOCUMENT-IDENTIFIER: US 5696127 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: December 9, 1997

US-CL-CURRENT: 514/285; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/252.04 ; 514/253.02 ; 514/255.05 ; 514/256 ; 514/267 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/338 ; 544/342 ; 544/344 ; 544/353 ; 546/62

APPL-NO: 08/ 465429

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned the entire disclosure of which is herein incorporated by reference.

US-PAT-NO: 5693647
DOCUMENT-IDENTIFIER: US 5693647 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: December 2, 1997

US-CL-CURRENT: 514/285; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/255.05 ; 514/256 ; 514/267 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/333 ; 544/342 ; 544/343 ; 544/344 ; 544/353 ; 546/62 ; 546/70 ; 546/77 ; 546/78

APPL-NO: 08/ 464546

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994 now abandoned, the entire disclosure of which is herein incorporated by reference.

US-PAT-NO: 5693646
DOCUMENT-IDENTIFIER: US 5693646 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: December 2, 1997

US-CL-CURRENT: 514/285; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/253.02 ; 514/256 ; 514/267 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/338 ; 544/342 ; 544/343 ; 544/344 ; 544/353 ; 546/62

APPL-NO: 08/ 464360

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994 abandoned, the entire disclosure of which is herein incorporated by reference.

US-PAT-NO: 5688810
DOCUMENT-IDENTIFIER: US 5688810 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: November 18, 1997

US-CL-CURRENT: 514/311; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/252.04 ; 514/255.05 ; 514/256 ; 514/267 ; 514/314 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/333 ; 544/338 ; 544/342 ; 544/353 ; 546/152 ; 546/167 ; 546/168 ; 546/173 ; 546/178 ; 546/180

APPL-NO: 08/ 464541

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned, the entire disclosure of which is herein incorporated by reference.

US-PAT-NO: 5688808
DOCUMENT-IDENTIFIER: US 5688808 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: November 18, 1997

US-CL-CURRENT: 514/285; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/252.04 ; 514/255.05 ; 514/256 ; 514/267 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/333 ; 544/342 ; 544/343 ; 544/344 ; 544/353 ; 546/62 ; 546/70 ; 546/77 ; 546/78

APPL-NO: 08/ 463231

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned the entire disclosure of which is herein incorporated by reference.

US-PAT-NO: 5521067
DOCUMENT-IDENTIFIER: US 5521067 A

TITLE: Bone marrow cell adhesion molecules and process for detecting adherence between cell adhesion molecules and cells generally

DATE-ISSUED: May 28, 1996

US-CL-CURRENT: 435/7.24; 435/29 ; 435/7.2 ; 435/7.9 ; 435/961 ; 435/962 ; 436/516 ; 436/63

APPL-NO: 08/ 158936

DATE FILED: November 24, 1993

PGPUB-DOCUMENT-NUMBER: 20020164663

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020164663 A1

TITLE: Methods and compositions for detection, diagnosis and prediction of antiestrogen-resistant breast cancer

PUBLICATION-DATE: November 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Fuqua, Suzanne A. W.	Sugarland	TX	US	
Friedrichs, William	Bergheim	TX	US	

APPL-NO: 09/ 877794

DATE FILED: June 8, 2001

RELATED-US-APPL-DATA:

child 09877794 A1 20010608 parent continuation-of PCT/US99/28206 19991129 US UNKNOWN non-provisional-of-provisional 60111428 19981208 US

US-CL-CURRENT: 435/7.23

ABSTRACT:

Disclosed are methods for the detection, diagnosis and prediction of tamoxifen-resistant breast cancer. Genetic and antibody probes and methods useful in determining the presence and monitoring the progression of breast cancer are also described. The methods involve determining polypeptide or mRNA expression of the genes encoding the angiogenic agents or receptors TIE-2, EDNRA, TGF.beta.3, TGFR.beta.III, VEGFR1, VEGF or bFGFR. Also described are procedures for combination therapies utilizing antiangiogenic agents or gene therapy directed towards TIE-2, EDNRA, TGF.beta.3, TGFR.beta.III, VEGFR1, VEGF or bFGFR, in combination with tamoxifen treatment of breast cancer.

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Detail Description Paragraph - DETX:

[0139] The airlift reactor, also initially described for microbial fermentation and later adapted for mammalian culture, relies on a gas stream to both mix and oxygenate the culture. The gas stream enters a riser section of the reactor and drives circulation. Gas disengages at the culture surface causing denser

of the reactor. The main advantage of this design is the simplicity and lack of need for mechanical mixing. Typically, the height-to-diameter ratio is 10:1. The airlift reactor scales up relatively easily, has good mass transfer of gases and generates relatively low shear forces.

Detail Description Paragraph - DETX:

[0172] In preferred embodiments, the probes or primers are labeled with radioactive species (.sup.32P, .sup.14C, .sup.35S, .sup.3H, or other label), with a fluorophore (rhodamine, fluorescein), or a chemilluminescent moiety (**luciferase**).

Detail Description Paragraph - DETX:

[0204] A preferred embodiment utilizes cDNA array technology, exemplified by the CLONTECH Atlas.TM. human cDNA expression array (CLONTECH Laboratories, Inc.). cDNA arrays offer the potential to simultaneously quantify expression of many genes. Advances in cDNA array technology to address array size, probe density, probe content and readout make this technology suitable for application in the laboratory (Marshall and Hodgson, 1998). However, the **novelty** of this technology means that there are no well-established and widely accepted standards to guide analysis and interpretation of the data. cDNA arrays have most often been utilized in paired comparisons (e.g. control vs. tumor) to identify differentially expressed genes in only a few types of cancer, such as melanoma (DeRisi et al., 1996), Ewing's sarcoma (Welford et al., 1998), alveolar rhabdomyosarcoma (Khan et al., 1998) and gastrointestinal tumors (Zhang et al., 1997). After standardization, rules for gene selection have typically been based on ratios of expression, for example, greater than two-fold difference (Schena et al., 1996), greater than three standard deviations of control genes ratio (DeRisi et al., 1996), or an arbitrary percent.

PGPUB-DOCUMENT-NUMBER: 20010010367

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20010010367 A1

TITLE: Luminescent gel coats and moldable resins

PUBLICATION-DATE: August 2, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Burnell-Jones, Peter	Burleigh Gardens		AU	

APPL-NO: 09/ 766415

DATE FILED: January 18, 2001

RELATED-US-APPL-DATA:

child 09766415 A1 20010118 parent division-of 09170432 19981013 US GRANTED
parent-patent 6207077 US

US-CL-CURRENT: 252/301.36

ABSTRACT:

Luminescent polymers are prepared from thermosetting unsaturated polyesters, suspending fillers and phosphorescent pigments and utilized to make gel coated articles and molded, cast and fiberglass reinforced plastic (FRP) articles. The luminescent polymers show bright and long-lasting photoluminescent afterglow, strong thermostimulation of afterglow by heat and electroluminescent properties. The preferred thermosetting unsaturated polyester resins are prepared by condensing mixtures of ethylenically unsaturated and aromatic dicarboxylic acids and anhydrides with dihydric alcohols and a polymerizable vinylidene monomer. Phthalic (orthophthalic) and isophthalic aromatic modified polyesters and their substituted derivatives are preferred, particularly those formed from maleate or fumarate unsaturated dicarboxylic acids and anhydrides and a glycol or mixtures of glycols. The preferred monomer is styrene. Preferred suspending fillers and thixotropic modifiers include silica, microspheres, glass fibers and other short fibers, nepheline syenite, feldspar, mica, pumice, magnesium sulfate, calcium carbonate, bentonite and the various clays and thixotropic modifiers and mixtures thereof. Preferred phosphorescent pigments include alkaline earth aluminate phosphors, zinc sulfide phosphors and mixtures of these phosphors. The luminescent resins may be rendered fire retardant and made flexible. As the heavy phosphorescent pigments remain in suspension, the raw luminescent resins are suitable for long-term storage and use.

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Summary of Invention Paragraph - BSTX:

[0005] Examples of luminescence are the dim glow of phosphorus (a chemiluminescence), the phosphorescence of certain solids (phosphors) after exposure to sunlight, X-rays or electron beams, the transitory fluorescence of many substances when excited by exposure to various kinds of radiation, the aurora borealis and the electroluminescence of gases when carrying a current, the triboluminescence of crystals when rubbed or broken, the **bioluminescence** of many organisms, including the firefly, the glowworm and the "burning of the sea," the fungus light of decaying tree trunks, and the bacterial light of dead flesh or fish.

Detail Description Paragraph - DETX:

[0131] JS AQUAGUARD Culture Finish/Clear Gelcoat is a clear polyester/styrene gel coat used as a topcoat for swimming pools containing fumed silica, benzophenone and/or phenolic UV inhibitors and metal naphthenates and octoates as activators. ESCON EX80 (61-286), obtained from FGI of Australia, is a low viscosity, low reactivity, high clarity, acrylic modified polyester resin designed for decorative castings and embedding where excellent color and clarity are desired. ESCON EX80 is supplied pre-accelerated and stabilized to minimize discoloration and deterioration by UV light. On the addition of 1% MEKP at 25.degree. C. a gel time of from 45-60 minutes can be expected. Curing proceeds relatively slowly once the resin has gelled; very low exotherm (approximately 40-50.degree. C.) characteristics give a slow even cure over a period of several hours, ensuring that cracking and discoloration due to overheating is avoided in larger casting. The low viscosity of ESCON EX80 is advantageous in allowing fast release of air **bubbles** before gelation occurs. Post curing of the finished article is essential.

Detail Description Paragraph - DETX:

[0194] Examples of the invention described above have been made and tested and found to deliver the advantages described. The luminescent polymers have been utilized as a gel coat on items including automobiles, hubcaps, bicycles (frame and wheel rims), signs, boats (exterior trim), trailers, outboard motor covers, fishing poles and banners. The luminescent polymers have been further utilized to mold items including safety and bicycle helmets, a dinghy runabout boat, house numbers and letters, keys for musical keyboards, skateboards, scratchplates for guitars, light switch and door handle surrounds, doors, smoke detector covers, knife and tool handles, telephones, floor tiles, ceiling and wall panels, stair treads, seat inserts and table tops, printed circuit boards, headlight and light reflectors, solar cell lens, spa baths and vanity basins, watch and clock faces, cats eye road markers, mouse and rat traps, flying insect catchers, walking sticks, lamp stands, remote controlled car bodies, battery covers for trucks, fishing lures, fiberglass rocks for use in spas and **novelty** items. Flexible items made and tested have included fishing nets

US-PAT-NO: 6462038

DOCUMENT-IDENTIFIER: US 6462038 B1

TITLE: Androgen receptor modulator compounds and methods

DATE-ISSUED: October 8, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Higuchi; Robert	Solana Beach	CA	N/A	N/A
Arienti; Kristen L.	San Diego	CA	N/A	N/A
Neelakandha; Mani	San Diego	CA	N/A	N/A
Pio; Barbara	San Diego	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A
Chen; Penghui	San Diego	CA	N/A	N/A
Caferro; Thomas R.	San Diego	CA	N/A	N/A

APPL-NO: 09/ 648684

DATE FILED: August 25, 2000

PARENT-CASE:

This application claims priority to U.S. Provisional Application Ser. No. 60/150,988, filed Aug. 27, 1999, the entire disclosure of which is incorporated by reference herein.

US-CL-CURRENT: 514/224.5; 514/229.8 ; 514/250 ; 514/291 ; 544/101 ; 544/34 ; 544/345 ; 546/80 ; 546/89 ; 546/90

ABSTRACT:

Compounds, pharmaceutical compositions, and methods for modulating processes mediated by steroid receptors. In particular, preparation and methods of use of non-steroidal compounds and compositions that are agonists, partial agonists, and antagonists for the androgen receptor (AR) are described. Further, described are the methods of making and use of critical intermediates including a stereoselective synthetic route to intermediates for the AR modulators.

69 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

These and various other advantages and features of **novelty** that characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. The following detailed description of the invention provides a better understanding of the invention, its advantages, and objects obtained by its use, as well as preferred embodiments of the invention.

Detailed Description Text - DETX:

General Method 14: Methenylation of a tertiary amide of Structure 16 and subsequent reduction with NaBH.sub.3 CN. To a solution of a substituted 7-isopropoxy-1-(2,2,2-trifluoroethyl)-9-(trifluoromethyl)-1H-[1,4]oxazino[3,2-g]quinolin-2(3H)-one derivative (1 equiv) in THF (0.15 M) was added Tebbe reagent (0.5 M in toluene, 1.1 equiv) at 0.degree. C. After 1 h, ether (50 mL/mmol) and methanol (0.7 mL/mmol) were added sequentially, and the brown solution was allowed to warm to rt. After 30 min, the mixture was filtered through Celite, rinsed with ether, and concentrated to a deep orange-brown solid. The solid was passed quickly through a plug of silica gel or basic alumina to afford an orange solid which was carried on directly. To a suspension of the above solid and NaBH.sub.3 CN (5 equiv) in dichloroethane (0.2 M) was added acetic acid (2.5 mL/mmol) dropwise at 0.degree. C. The mixture **bubbled** vigorously, and was allowed to warm to rt. After 1 d the orange solution was poured into NaHCO.sub.3 (40 mL/mmol) and extracted with EtOAc (2.times.40 mL/mmol). The organic layers were washed with brine (30 mL/mmol), dried over MgSO.sub.4, filtered, and concentrated. The material was purified as indicated.

Detailed Description Text - DETX:

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX:

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be conveniently measured, e.g., by increasing **luciferase** production, which

To detect antagonists, the co-transfection assay is carried out in the presence of a constant concentration of an agonist to the target IR (e.g., progesterone for PR) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., **luciferase** production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing an androgen response element. See e.g., Berger et al. supra. In addition, pRS-.beta.-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 6448405

DOCUMENT-IDENTIFIER: US 6448405 B1

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: September 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jones; Todd K.	Solana Beach	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A
Edwards; James P.	San Diego	CA	N/A	N/A
Tegley; Christopher M.	San Diego	CA	N/A	N/A
West; Sarah J.	San Diego	CA	N/A	N/A

APPL-NO: 08/ 947428

DATE FILED: October 8, 1997

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is divisional of 08,465,429, filed on Jun. 5, 1995, U.S. Pat. No. 5,696,127, which is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994, now abandoned the entire disclosure of which is herein incorporated by reference.

US-CL-CURRENT: 546/62; 549/390

ABSTRACT:

Non-steroidal compounds which are high affinity, high selectivity modulators for steroid receptors are disclosed. Also disclosed are pharmaceutical compositions incorporating such compounds, methods for employing the disclosed compounds and compositions for treating patients requiring steroid receptor agonist or antagonist therapy, intermediates useful in the preparation of the compounds and processes for the preparation of the steroid receptor modulator compounds.

4 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Brief Summary Text - BSTX:

the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX:

To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg, 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was **bubbled** through the colorless solution for 15 min. The solution was cooled to 0.degree. C. in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was placed in an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50%) of 5-Fluoro-3-nitroiodobenzene. Data for 5-Fluoro-3-nitroiodobenzene: .sup.1 H NMR (400 MHz, acetone-d.sub.6) 8.36 (s, 1H), 8.00 (m, 2H).

Detailed Description Text - DETX:

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX:

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be conveniently measured, e.g., by increasing **luciferase** production, which reflects compound-dependent, IR-mediated increases in reporter transcription. To detect antagonists, the co-transfection assay is carried out in the presence of a constant concentration of an agonist to the target IR (e.g., progesterone for PR) known to induce a defined reporter signal. Increasing concentrations

production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing a progesterone response element. This plasmid is more fully described in Berger et al. supra. In addition, for ER agonist and antagonist determinations, the reporter plasmid MTV-ERE5-LUC, which contains LUC under control of the mouse mammary tumor virus (MTV) long terminal repeat in which the glucocorticoid response elements have been deleted and replaced with five copies of a 33-base pair ERE as described in Tzukerman et al., supra, was substituted for the MTV-LUC plasmid described herein. pRS- beta -Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 6121450

DOCUMENT-IDENTIFIER: US 6121450 A

TITLE: Intermediates for preparation of steroid receptor modulator compounds

DATE-ISSUED: September 19, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jones; Todd K.	Solana Beach	CA	N/A	N/A
Winn; David T.	San Diego	CA	N/A	N/A
Hamann; Lawrence G.	San Diego	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A
Farmer; Luc J.	La Jolla	CA	N/A	N/A
Davis; Robert L.	Santee	CA	N/A	N/A

APPL-NO: 08/ 947427

DATE FILED: October 8, 1997

PARENT-CASE:

RELATED PATENT APPLICATIONS This is a divisional of copending application Ser. No. 08/462,643, filed on Jun. 5, 1995, which is in turn a Continuation-In-Part of Ser. No. 08/363,529, filed Dec. 22, 1994 now abandoned.

US-CL-CURRENT: 546/81

ABSTRACT:

Non-steroidal compounds which are high affinity, high selectivity modulators for steroid receptors are disclosed. Also disclosed are pharmaceutical compositions incorporating such compounds, methods for employing the disclosed compounds and compositions for treating patients requiring steroid receptor agonist or antagonist therapy, intermediates useful in the preparation of the compounds and processes for the preparation of the steroid receptor modulator compounds.

2 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Brief Summary Text - BSTX:

the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX

5-Fluoro-3-nitroiodobenzene To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg, 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was **bubbled** through the colorless solution for 15 min. The solution was cooled to 0.degree. C. in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was placed in an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50%) of 5-fluoro-3-nitroiodobenzene. Data for 5-fluoro-3-nitroiodobenzene: sup.1 H NMR (400 MHz, acetone-d6) 8.36 (s, 1 H), 8.00 (m, 2 H).

Detailed Description Text - DETX

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to incude cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX:

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be conveniently measured, e.g., by increasing **luciferase** production, which reflects compound-dependent, IR-mediated increases in reporter transcription. To detect antagonists, the co-transfection assay is carried out in the presence of a constant concentration of an agonist to the target IR (e.g., progesterone for PR) known to induce a defined reporter signal. Increasing concentrations

producton). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing a progesterone response element. This plasmid is more fully described in Berger et al. supra. In addition, for ER agonist and antagonist determinations, the reporter plasmid MTV-ERE5-LUC, which contains LUC nder control of the mouse mammary tumor virus (MTV) long terminal repeat in which the glucocorticoid response elements have been deleted and replaced with five copies of a 33-base pair ERE as described in Tzukerman et al., supra, was substituted for the MTV-LUC plasmid described herein. pRS-.beta.-Gal, coding for constitutive

US-PAT-NO: 6093821

DOCUMENT-IDENTIFIER: US 6093821 A

TITLE: Process for preparing steroid receptor modulator compounds

DATE-ISSUED: July 25, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jones; Todd K.	Solana Beach	CA	N/A	N/A
Goldman; Mark E.	San Diego	CA	N/A	N/A
Pooley; Charlotte L. F.	San Diego	CA	N/A	N/A
Winn; David T.	San Diego	CA	N/A	N/A
Edwards; James P.	San Diego	CA	N/A	N/A
West; Sarah J.	San Diego	CA	N/A	N/A
Tegley; Christopher M.	San Diego	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A

APPL-NO: 08/ 943853

DATE FILED: October 8, 1997

PARENT-CASE:

RELATED PATENT APPLICATIONS This is a divisional of application(s) Ser. No. 08/464,541, filed on Jun. 5, 1995 U.S. Pat. No. 5,688,810, which is in turn a Continuation-In-Part of Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned.

US-CL-CURRENT: 544/333; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/249 ; 544/284 ; 544/338 ; 544/342 ; 544/344 ; 544/353 ; 546/152 ; 546/153 ; 546/159 ; 546/165 ; 546/167 ; 546/168 ; 546/173 ; 546/178 ; 546/179 ; 546/180

ABSTRACT:

Non-steroidal compounds which are high affinity, high selectivity modulators for steroid receptors are disclosed. Also disclosed are pharmaceutical compositions incorporating such compounds, methods for employing the disclosed compounds and compositions for treating patients requiring steroid receptor agonist or antagonist therapy, intermediates useful in the preparation of the compounds and processes for the preparation of the steroid receptor modulator compounds.

12 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Brief Summary Text - BSTX:

These and various other advantages and features of **novelty** which characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX:

To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg, 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was **bubbled** through the colorless solution for 15 min. The solution was cooled to 0.degree. C. in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was placed in an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50%) of 5-fluoro-3-nitroiodobenzene. Data for 5-fluoro-3-nitroiodobenzene: .sup.1 H NMR (400 MHz, acetone-d6) 8.36 (s, 1 H), 8.00 (m, 2 H).

Detailed Description Text - DETX:

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmids functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX:

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound

conveniently measured, e.g., by increasing **luciferase** production, which reflects compound-dependent, IR-mediated increases in reporter transcription. To detect antagonists, the co-transfection assay is carried out in the presence of a constant concentration of an agonist to the target IR (e.g., progesterone for PR) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., **luciferase** production). The co-transfection assay is therefore useful to detect both agonists and antagonist of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing a progesterone response element. This plasmid is more fully described in Berger et al. supra. In addition, for ER agonist and antagonist determinations, the reporter plasmid MTV-ERE5-LUC, which contains LUC under control of the mouse mammary tumor virus (MTV) long terminal repeat in which the glucocorticoid response elements have been deleted and replaced with five copies of a 33-base pair ERE as described in Tzukerman et al., supra, was substituted for the MTV-LUC plasmid described herein. pRS-.beta.-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 5994544

DOCUMENT-IDENTIFIER: US 5994544 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: November 30, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jones; Todd K.	Solana Beach	CA	N/A	N/A
Tegley; Christopher M.	San Diego	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A
Edwards; James P.	San Diego	CA	N/A	N/A

APPL-NO: 08/ 947413

DATE FILED: October 8, 1997

PARENT-CASE:

RELATED PATENT APPLICATIONS This is a divisional of application Ser. No. 08/464,360, filed on Jun. 5, 1995, U.S. Pat. No. 5,693,646, which is in turn a Continuation-In-Part of Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned.

US-CL-CURRENT: 546/62; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/342 ; 544/343 ; 544/344 ; 544/353 ; 544/383

ABSTRACT:

Non-steroidal compounds which are high affinity, high selectivity modulators for steroid receptors and the method of preparing these compounds are disclosed. Also disclosed are pharmaceutical compositions incorporating such compounds, methods for employing the disclosed compounds and compositions for treating patients requiring steroid receptor agonist or antagonist therapy, intermediates useful in the preparation of the compounds and processes for the preparation of the steroid receptor modulator compounds.

1 Claims. 0 Drawing figures

Exemplary Claim Number: 1

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Brief Summary Text - BSTX:

These and various other advantages and features of **novelty** which characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX:

6-(5-Fluoro-3-nitrophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound 280, structure 4 of Scheme II, where R.sup.1 .dbd.5-fluoro-3-nitrophenyl) 1-Fluoro-3-nitroidobenzene To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was **bubbled** through the colorless solution for 15 min. The solution was cooled to 0.degree. C. in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was place din an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50%) of 5-fluoro-3-nitroiodobenzene. Data for 5-fluoro-3-nitroiodobenzene: .sup.1 H NMR (400 MHz, acetone-d6) 8.36 (s, 1 H), 8.00 (m, 2 H).

Detailed Description Text - DETX:

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR, or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX:

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be conveniently measured, e.g., by increasing **luciferase** production, which reflects compound-dependent, IR-mediated increases in reporter transcription

of a constant concentration of an agonist to the target IR (e.g., progesterone for PR) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., **luciferase** production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing a progesterone response element. This plasmid is more fully described in Berger et al. supra. In addition, for ER agonist and antagonist determinations, the reporter plasmid MTV-ERE5-LUC, which contains LUC under control of the mouse mammary tumor virus (MTV) long terminal repeat in which the glucocorticoid response elements have been deleted and replaced with five copies of a 33-base pair ERE as described in Tzukerman et al., supra, was substituted for the MTV-LUC plasmid described herein. pRS-.beta.-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 5879894

DOCUMENT-IDENTIFIER: US 5879894 A

TITLE: Long emission wavelength chemiluminescent compounds and their use in test assays

DATE-ISSUED: March 9, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Law; Say-Jong	Westwood	MA	N/A	N/A
Jiang; Qingping	Northborough	MA	N/A	N/A
Fischer; Walter	Reinach	N/A	N/A	CH
Unger; John T.	Medfield	MA	N/A	N/A
Krodel; Elizabeth K.	Arlington	MA	N/A	N/A
Xi; Jun	North Quincy	MA	N/A	N/A

APPL-NO: 08/ 308772

DATE FILED: September 19, 1994

PARENT-CASE:

This is a continuation-in-part application of application Ser. No. 08/035,130, filed on Mar. 19, 1993, now U.S. Pat. No. 5,395,752.

US-CL-CURRENT: 435/7.1; 436/172 ; 436/501 ; 436/536

ABSTRACT:

An assay method incorporating at least two different chemiluminescent compounds for detection and/or quantitation of at least two substances in a test sample is described. The synthesis of chemiluminescent reagents or conjugates for use in such methods as well as kits incorporating such reagents are also disclosed. The assays have particular application in the field of clinical diagnostics.

13 Claims. 62 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 49

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Detailed Description Text - DETX:

A mixture of -12-chloro-benz[b]acridine (2.3 g, 8.68 mmol), potassium cyanide (620 mg, 9.55 mmol) and copper(I) cyanide (391 mg, 4.43 mmol) in anhydrous methanol (16 ml) was **bubbled** with nitrogen for 1 minute and then kept in a sealed tube. The mixture was heated at 160.degree. C. with stirring for 4.5 hours and cooled. The red-brown mixture was evaporated and the residue was flash-chromatographed (W.C. still et al: J. Org. Chem., 43, 2923, (1978)) on a silica column (Baker silica gel, Cat# 7024-1) packed with hexane and eluted with 10% ethyl acetate-hexane, yielding red 12-cyano-benz[b]acridine (1.54 g, 70%). Rf 0.7 (silica gel, hexane/ethyl acetate 2:1). MS (FAB, Thioglycerol Matrix): m/z 255 (M+1).

Detailed Description Text - DETX:

To an iced cooled solution of 2-dimethylamino ethylchloride hydrochloride (10.48 g, 72.72 mmol) in 30 ml of water, a solution of NaOH (3.49 g, 87.26 mmol) in 20 ml of water was added. After 30 min stirring, the reaction was saturated with NaCl for 15 min and extracted with toluene (5.times.50 ml). The toluene fractions were combined and dried over KOH pellets. In a separate flask, a mixture of KOH (4.07 g, 72.72 mmol) and 4-indophenol (16 g, 72.72 mmol) in 48 ml of anhydrous ethanol was stirred at room temperature for 1.5 hours and evaporated under vacuo to give the 4-iodophenoxide salt as a greenish oily residue. The above dimethylaminoethyl chloride in toluene solution was then added to the 4-iodophenoxide residue and the mixture refluxed with stirring at 120.degree. C. for 21 hours. The reaction mixture was cooled down and filtered. The filtrate was evaporated and the residue redissolved in 200 ml of ether. After filtration, the filtrate was **bubbled** with HCl gas to give a copious white precipitate, which was then filtered and dried to give the p-N,N-dimethylaminoethoxy 4-iodobenzene hydrogen chloride as white solid (11 g, yield 46.2%).

Detailed Description Text - DETX:

It is to be understood that various other modifications will be apparent to and can readily be made by those skilled in the art, given the disclosure herein, without departing from the scope and materials of this invention. It is not, however, intended that the scope of the claims appended hereto be limited to the description as set forth herein, but rather that the claims be construed as encompassing all features of patentable **novelty** which reside in the present invention, including all features which would be treated as equivalents thereof by those skilled in the art to which the invention pertains. It is also noted that the examples given therein are intended to illustrate, and not to limit the invention.

Other Reference Publication - OREF:

Edwards et al., "Unusual Luminescent Properties of Odd-and Even-substituted Naphythyl-derivatized Dioxetanes," Journal of **Bioluminescence** and Chemiluminescence, 5:1-4, 1990.

Other Reference Publication - OREF:

McCapra, F., "Chemical Mechanisms in **Bioluminescence,**" Accounts of Chemical Research, 9:201-208, 1976.

Other Reference Publication - OREF:

McCapra et al., "Luminescent Labels for Immunoassay--From Concept to Practice," Journal of **Bioluminescence** and Chemiluminescence, 4:51-58, 1989.

Other Reference Publication - OREF:

Wood et al., "**Bioluminescent** Click Beetles Revisited" Journal of **Bioluminescence** and Chemiluminescence, 4:31-39, 1989.

Other Reference Publication - OREF:

5.sup.th International Symposium on **Bioluminescence** and Chemiluminescence, Florence-Bologna, Italy, Sep. 25-29, 1988, Poster. Edwards et al.

Other Reference Publication - OREF:

5.sup.th International Symposium on **Bioluminescence** and Chemiluminescence, Florence-Bologna, Italy, Sep. 25-29, 1988, Finale Programme.

Other Reference Publication - OREF

Kinkel, et al., "Synthesis and Properties of New Luminescent Acridinium-9-carboxylic Acid Derivatives and their Application in Luminescence Immunoassays (LIA)", Journal of **Bioluminescence** and Chemiluminescence, 4:136-139, 1989.

Other Reference Publication - OREF

Mattingly, P., "Chemiluminescent 10-Methyl-Acridinium-9-(N-Sulphonylcarboxamide) Salts. Synthesis and Kinetics of Light Emission", Journal of **Bioluminescence** and Chemiluminescence, 6:107-114, 1991.

US-PAT-NO: 5780239

DOCUMENT-IDENTIFIER: US 5780239 A

TITLE: Method for the determination of cast in urine

DATE-ISSUED: July 14, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Carter; Jesse M.	Tampa	FL	33606	N/A
Smith; Jack V.	St. Petersburg	FL	33709	N/A

APPL-NO: 08/ 675386

DATE FILED: July 2, 1996

PARENT-CASE:

PRIOR APPLICATIONS This application is a continuation in part of application Ser. No. 08/347,124, filed Nov. 23, 1994, now abandoned.

US-CL-CURRENT: 435/7.1; 435/7.9 ; 436/518 ; 436/87

ABSTRACT:

Method for detecting casts in urine by measuring Tamm-Horsfall protein by solid and liquid phase reagents including a method for manufacturing a enzyme specific for Tamm-Horsfall protein which produces a detectable response in the presence of casts in urine.

1 Claims, 0 Drawing figures

Exemplary Claim Number: 1

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Brief Summary Text - BSTX:

A thorough search of patents and research revealed no relative art (i.e., prior art) showing any correlation to this technology. The art of manual microscopic analysis aside, no chemical test means has been described prior to this art for this method. However, the following art will be mentioned to further illustrate the **novelty** of the present art and the advancement to the art the present device yields. The following patents with the exception of U.S. Pat. No. 4,575,486, do not mention any use of urine as the matrix for detecting specific analytes of interest. It is known in the art that the urine matrix is

buffering and interference problems (cannibal like enzymes such as protease) that have to be overcome to provide a method that can be used for the general population with precision and accuracy. The mere mention of a technique that can test a fluid does not include the area of complex fluids such as urine and cannot be used in the same context.

Brief Summary Text - BSTX:

3. Enzyme-labeled antibodies or antigens (indicators)--antibodies for THP are known in the art. It is also known in the art that antibodies can be labeled. The preferred antibody label in the present device can be labeled with nicotinamide adenine dinucleotide phosphate, reduced form (NADPH), nicotinamide adenine dinucleotide phosphate (NADP+), nicotinamide adenine dinucleotide (NAD), nicotinamide adenine dinucleotide, reduced form (NADH), glucose-6-phosphate dehydrogenase (G-6-PDH), alkaline phosphatase, glycerol kinase, beta-delta-galactosidase, C-reactive protein, N- acetylneuraminic acid aldolase, Acyl-CoA oxidase, Acyl-CoA synthetase, Acylpolyamine amidohydrolase, Alcohol oxidase, Alkaline phosphatase, Alkalophilic proteinase, Ascorbate oxidase, cholesterol esterase, cholesterol oxidase, choline oxidase, creatine amidinohydrolase, Creatinine amidohydrolase, creatinine diminase, Diaphorase, Formaldehyde dehydrogenase, delta-Fructose dehydrogenase, Galactose oxidase, beta-Glactosidase, Glucose dehydrogenase, Glucose oxidase, alpha-Glucosidase, beta-Glucosidase, Glutamate dehydrogenase, Glutathione peroxidase, Glucoamlyase, Glycerol dehydrogenase, Glycerol-3-phosphate dehydrogenase, Glycerol kinase, Glycerophosphate oxidase, Hexokinase, para-Hydroxybenzoate hydroxylase, delta-3-Hydroxybutyrate dehydrogenase, Invertase, lactate dehydrogenase, Leucine dehydrogenase, Lipoprotein lipase, Lipase, Amylase, **Luciferase,** Malate dehydrogenase, Mannitol dehydrogenase, NADPH oxidoreductase, Neuraminidase, Peroxidase, Urease, Uricase, Xanthine oxidase, europium chelate, Protease or other label. For example, in the analysis of urine for THP on an automated instrument, the THP liquid reagent containing anti-THP-G-6-PDH binds with THP (if present in the urine) in the presence of NAD+ and glucose, NADH will be formed, this corresponding reduction of NAD+ to NADH can be measured quantitatively at 340 nanometers (ultra-violet (UV)). In the alternative, for the analysis of urine for THP on a dipstick, the THP test strip reagent containing anti-THP-Glucose oxidase binds with THP (if present in the urine) in the presence of glucose, peroxidase, and 2,2'-Azinobis(3-ethylbenzthiazoline) sulfonic acid (ABTS, reduced, is colorless chromogenic oxygen acceptor), hydrogen peroxide will be formed from the oxidation of glucose by glucose oxidase, the hydrogen peroxide is then oxidized by the peroxidase and oxygen is given off, the ABTS (present) accepts the oxygen and is oxidized (blue color formed), this corresponding development of color can be measured semi-quantitatively on the dipstick.

Brief Summary Text - BSTX:

As a wetting agent, there is preferably used a long chain organic sulphate or sulphonate, for example sodium dodecyl-benzene sulphonate, BRIJ-35 30% w/v solution of polyoxyethylene ethers, TWEEN 20 polyoxyethylenesorbitan, dioctyl sodium sulphosuccinate or sodium laural sulphate, etc., which are known to

solution in amounts of 0.5 to 5 percent, preferably of 1-3 percent. The wetting agents also aid in solubility and reduction of **bubbles** in solution which is critical in the liquid chemistry rapid test for casts.

Detailed Description Text - DETX:

In closing, to further explain test strip method and use for the determining the presence of Tamm-Horsfall protein in a urine sample, the test strip can comprise of a matrix material comprising a test area impregnated with an indicator reagent selected from the group consisting of ion-exchange, labeled antibody, labeled antigen, chromogenic, Tamm-Horsfall glycoprotein specific and enzymatic indicators and buffers. Also, this test strip for the determining the presence of Tamm-Horsfall protein in the urine sample, can comprise a matrix material comprising a test area impregnated with a indicator reagent selected from the group consisting of ion-exchange, labeled antibody, labeled antigen, chromogenic, and enzymatic indicators, buffers and substrates, and dipping the test strip into the urine sample containing Tamm-Horsfall protein, and determining by measurement of a detectable response by reflectance, visual, colorimetric and spectrophotometric means. This test strip can have series of different types of indicators not to exclude the following, THP specific indicator reagents selected from the group consisting of Tamm-Horsfall red, Tamm-Horsfall blue, Tamm-Horsfall green and Tamm-Horsfall yellow, Tamm-Horsfall ion-exchange indicator reagents selected from the group consisting of Tamm-Horsfall polyvinyl and Tamm-Horsfall ethyleneglycol-bis(beta-aminoethyl ether)N,N,N',N'-tetraacetic acid, and Tamm-Horsfall labeled antibody or antigen indicator reagent labels are selected from the group consisting of nicotinamide adenine dinucleotide phosphate, reduced form (NADPH), nicotinamide adenine dinucleotide phosphate, nicotinamide adenine dinucleotide, nicotinamide adenine dinucleotide, reduced form, glucose-6-phosphate dehydrogenase, alkaline phosphatase, glycerol kinase, beta-delta-galactosidase, C-reactive protein, N-acetylneuraminic acid aldolase, Acyl-CoA oxidase, Acyl-CoA synthetase, Acylpolyamine amidohydrolase, Alcohol oxidase, Alkaline phosphatase, Alkalophilic proteinase, Ascorbate oxidase, cholesterol esterase, cholesterol oxidase, choline oxidase, creatine amidinohydrolase, Creatinine amidohydrolase, creatinine diminase, Diaphorase, Formaldehyde dehydrogenase, delta-Fructose dehydrogenase, Galactose oxidase, beta-Glactosidase, Glucose dehydrogenase, Glucose oxidase, alpha-Glucosidase, beta-Glucosidase, Glutamate dehydrogenase, Glutathione peroxidase, Glucoamlyase, Glycerol dehydrogenase, Glycerol-3-phosphate dehydrogenase, Glycerol kinase, Glycerophosphate oxidase, Hexokinase, para-Hydroxybenzoate hydroxylase, delta-3-Hydroxybutyrate dehydrogenase, Invertase, lactate dehydrogenase, Leucine dehydrogenase, Lipoprotein lipase, Lipase, Amylase, **Luciferase,** Malate dehydrogenase, Mannitol dehydrogenase, NADPH oxidoreductase, Neuraminidase, Peroxidase, Urease, Uricase, Xanthine oxidase, europium chelate and Protease, and Tamm-Horsfall chromogenic indicator reagents are selected from the group consisting of 4-aminoantipyrine, ABTS, para-Nitrophenyl phosphate, 5-Bromo-4-chloro-3-indoyl phosphate, 3,3',5,5'-Tetramethylbenzidine, ortho-Dianisidine, 5-Aminosalicylic acid, 3,3'-Diaminibenzidine, 3-Amino-9-Ethylcarbazole, 4-Chloro-1-napthol,4-Chloro-2-methylbenzenediazonium salt, Napthol AS-TR phosphate, Azoalbumin, p-Nitrophenylphosphate, 2,6-dichloropehnol-indophenol, nitrotetrazorium blue, ortho-nitrophenyl, NAD, NADP, NADPH, pyrogallo

enzymatic indicator reagents selected from the group consisting of Tamm-Horsfall protine dehydrogenase, Tamm-Horsfall protein oxidase, Tamm-Horsfall protein hydrolase, Tamm Horsfall protein oxidoreductase and Tamm-Horsfall proteinase, also buffers can be selected from the group consisting of citrate, tris(hydroxymethyl)aminomethane) (TRIS), phosphate, phthalate, acetate, hydrochloric acid, N-2-Hydroxyethylpiperazine-N'-2-ethanesulfonic acid, 2-(N-Morpholino)-ethanesulfonic acid, 3-(N-Morpholino)propanesulfonic acid, [Piperazine-N,N'-bis(ethanesulfonic acid)], 3-(Cyclohexylamino)-2-hydroxy-1-propanesulfonic acid, 3-[N,N-bis(hydroxyethyl)amino]-2-hydroxypropanesulfonic acid, Piperazine-N,N'-bis(2-hydroxypropanesulfonic acid), 3-[N-tris-(hydroxymethyl)methyl amino]-2-hydroxypropanesulfonic acid, [3-[(1,1-Dimethyl-hydroxyethyl)amino]-2-hydroxypropanesulfonic acid], oxalate, citrate and succinate. And substrates can be selected from the group consisting of vitamin C, Acyl-CoA, Alcohol, Alkaline phosphatase, cholesterol, choline, creatine, creatinine, formaldehyde, fructose, galactose, glucose, glutamate, 1,2-phenylenediaminehydrochloride, ortho-phenylenediamine, glycerol, lactate, lipoprotein, malate, mannitol, hydrogen peroxide, proline, pyruvate, sarcosine, sorbitol, urea, phenol, xanthine among others, finally the method for determining the presence of Tamm-Horsfall protein on a test strip impregnated with a Tamm-Horsfall indicator and buffer comprising the steps of dipping a test strip into a urine sample containing Tamm-Horsfall protein and determining the color change by reflectance, visual, calorimetric and spectrophotometric means.

Detailed Description Text - DETX

And, to further explain liquid reagent method and use for the determining the presence of Tamm-Horsfall protein in a urine sample, the liquid reagent can comprise of a an indicator reagent selected from the group consisting of ion-exchange, labeled antibody, Tamm-Horsfall glycoprotein specific, labeled antigen, chromogenic, enzymatic indicators and buffers. Also, this liquid reagent for the determining the presence of Tamm-Horsfall protein in the urine sample, can comprise of indicator reagents selected from the group consisting of ion-exchange, labeled antibody, labeled antigen, chromogenic, and enzymatic, buffers and substrates, and determining by color change by reflectance, visual, UV, calorimetric and spectrophotometric (specifically ultra-violet) means. This liquid reagent can have series of different types of indicators not to exclude the following. THP specific indicator reagents selected from the group consisting of Tamm-Horsfall red, Tamm-Horsfall blue, Tamm-Horsfall green and Tamm-Horsfall yellow, Tamm-Horsfall ion-exchange indicator reagents selected from the group consisting of Tamm-Horsfall polyvinyl and Tamm-Horsfall ethyleneglycol-bis(beta-aminoethyl ether)N,N,N',N'-tetraacetic acid, and Tamm-Horsfall labeled antibody or antigen indicator reagent labels are selected from the group consisting of nicotinamide adenine dinucleotide phosphate, reduced form (NADPH), nicotinamide adenine dinucleotide phosphate, nicotinamide adenine dinucleotide, nicotinamide adenine dinucleotide, reduced form, glucose-6-phosphate dehydrogenase, alkaline phosphatase, glycerol kinase, beta-delta-galactosidase, C-reactive protein, N-acetylneuraminic acid aldolase, Acyl-CoA oxidase, Acyl-CoA synthetase, Acylpolyamine amidohydrolase, Alcohol

cholesterol esterase, cholesterol oxidase, choline oxidase, creatine amidinohydrolase, Creatinine amidohydrolase, creatinine diminase, Diaphorase, Formaldehyde dehydrogenase, delta-Fructose dehydrogenase, Galactose oxidase, beta-Glactosidase, Glucose dehydrogenase, Glucose oxidase, alpha-Glucosidase, beta-Glucosidase, Glutamate dehydrogenase, Glutathione peroxidase, Glucoamlyase, Glycerol dehydrogenase, Glycerol-3-phosphate dehydrogenase, Glycerol kinase, Glycerophosphate oxidase, Hexokinase, para-Hydroxybenzoate hydroxylase, delta-3-Hydroxybutyrate dehydrogenase, Invertase, lactate dehydrogenase, Leucine dehydrogenase, Lipoprotein lipase, Lipase, Amylase, **Luciferase,** Malate dehydrogenase, Mannitol dehydrogenase, NADPH oxidoreductase, Neuraminidase, Peroxidase, Urease, Uricase, Xanthine oxidase, europium chelate, 7-amido-4-methylcoumarin and Protease, and Tamm-Horsfall chromogenic indicator reagents are selected from the group consisting of 4-aminoantipyrine, ABTS, para-Nitrophenyl phosphate, 7-amido-4-methylcoumarin 5-Bromo-4-chloro-3-indoyl phosphate, 3,3',5,5'-Tetramethylbenzidine, ortho-Dianisidine, 5-Aminosalicylic acid, 3,3'-Diaminibenzidine, 3-Amino-9-Ethylcarbazole, 4-Chloro-1-napthol,4-Chloro-2-methylbenzenediazonium salt, Napthol AS-TR phosphate, Azoalbumin, p-Nitrophenylphosphate, 2,6-dichloropehnol-indophenol, nitrotetrazorium blue, ortho-nitrophenyl, NAD, NADP, NADPH, pyrogallo, para-nitroanilide, hypoxanthine, cytochrome C and uric acid, and Tamm-Horsfall enzymatic indicator reagents selected from the group consisting of Tamm-Horsfall protein dehydrogenase, Tamm-Horsfall protein oxidase, Tamm-Horsfall hydrolase, Tamm Horsfall protine oxidoreductase and Tamm-Horsfall proteinase, also buffers can be selected from the group consisting of citrate, tris(hydroxymethyl)aminomethane) (TRIS), phosphate, phthalate, acetate, hydrochloric acid, N-2-Hydroxyethylpiperazine-N'-2-ethanesulfonic acid, 2-(N-Morpholino)-ethanesulfonic acid, 3-(N-Morpholino)propanesulfonic acid, [Piperazine-N,N'-bis(ethanesulfonic acid)], 3-(Cyclohexylamino)-2-hydroxy-1-propanesulfonic acid, 3-[N,N-bis(hydroxyethyl)amino]-2-hydroxypropanesulfonic acid, Piperazine-N,N'-bis(2-hydroxypropanesulfonic acid), 3-[N-tris-(hydroxymethyl)methyl amino]-2-hydroxypropanesulfonic acid, [3-[(1,1-Dimethyl-hydroxyethyl)amino]-2-hydroxypropanesulfonic acid], oxalate and succinate are selected from the group consisting of citrate, and substrates can be selected from the group consisting of vitamin C, Acyl-CoA, Alcohol, Alkaline phosphatase, cholesterol, choline, creatine, creatinine, formaldehyde, fructose, galactose, glucose, glutamate, 1,2-phenylenediaminehydrochloride, ortho-phenylenediamine, glycerol, lactate, lipoprotein, malate, mannitol, hydrogen peroxide, praline, pyruvate, sarcosine, sorbitol, urea, phenol, xanthine among others, finally the method for determining the presence of Tamm-Horsfall protein on a test strip impregnated with a Tamm-Horsfall indicator and buffer comprising the steps of dipping a test strip into a urine sample containing Tamm-Horsfall protein and determining the color change by reflectance, visual, calorimetric and spectrophotometric means. The method for determining the presence of Tamm-Horsfall protein in a urine comprising placing an aliquot of the urine to be tested in an automated analyzer sampling cup, placing the cup in a sampling tray within the automated analyzer, transferring the urine to a cuvette mounted within the automated analyzer, injecting at least one reagent composition in an aqueous medium into the cuvette, wherein said at least one reagent composition comprises a buffer to adjust the pH of the reaction solution to a preferred pH, a Tamm-Horsfall indicator reagent, reading the aliquot of urine at specified intervals, in accordance with a

monochromatically specified wavelength, to compare absorbance of the patient's urine and reagent composition complex with that of a standard containing a known concentration of Tamm-Horsfall protein and thereby determining the presence or absence of cast in the patient's urine.

US-PAT-NO: 5770383

DOCUMENT-IDENTIFIER: US 5770383 A

TITLE: Tricyclic retinoids, methods for their production and use

DATE-ISSUED: June 23, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hwang; Chan Kou	Boulder	CO	N/A	N/A
White; Steven K.	San Diego	CA	N/A	N/A
Bennani; Youssef L.	La Jolla	CA	N/A	N/A
Canan Koch; Stacie S.	San Diego	CA	N/A	N/A
Badea; Beth Ann	San Diego	CA	N/A	N/A
Hebert; Jonathan J.	Mission Viejo	CA	N/A	N/A
Farmer; Luc J.	La Jolla	CA	N/A	N/A
Nadzan; Alex M.	San Diego	CA	N/A	N/A

APPL-NO: 08/ 475397

DATE FILED: June 7, 1995

PARENT-CASE:

REFERENCE TO RELATED APPLICATIONS This application is a Continuation-In-Part application of U.S. patent application Ser. No. 08/366,630, filed Dec. 30, 1994, now abandoned, the entire disclosure of which is herein incorporated by reference.

US-CL-CURRENT: 435/7.1; 514/217 ; 514/290 ; 514/454 ; 514/510 ; 514/569 ; 530/350 ; 530/369 ; 530/412 ; 540/586 ; 546/101 ; 549/388 ; 560/8 ; 562/405

ABSTRACT:

Tricyclic retinoids having activity for retinoic acid receptors and/or retinoid X receptors are provided. Also provided are pharmaceutical compositions incorporating such tricyclic retinoid compounds and methods for their therapeutic use.

39 Claims. 0 Drawing figures

Exemplary Claim Number: 1

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Brief Summary Text - BSTX:

These and various other advantages and features of **novelty** which characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. Ilowever, for a better understanding of the invention, its advantages, and(i objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX:

A 50 mL round-bottom flask was flame-dried and charged with anhydrous THF (10 mL) and ethyl magnesium bromide (2.65 mL of 1M solution in THF, 2.65 mM) and the structure was cooled to 0.degree. C. Under a nitrogen atmosphere, a solution of ethyl ethynyl ether (0.375 mL of a 50% solution in hexanes, Aldrich Inc., 2.63 mM) was slowly added. The crude mixture was warmed to room temperature and stirred for 20 min. A solution of 4,4,5,5,8,8-hexamethyl-1,2,3,4,5,6,7,8-octahydroanthracen-1-one (0.50 g, 1.76 mmol) in THF (10 mL) was slowly added and stirring was continued for 2 h. The reaction mixture was quenched with a sat. solution of ammonium chloride and extracted with diethyl ether. The organic layer was dried over MgSO.sub.4, and the solvent evaporated. The crude residue was dissolved in ethanol (20 mL) and CO.sub.2 (dry ice) was **bubbled** through the solution for 3 h. After stirring for 12 h at 25.degree. C., the solvent was evaporated and the residue was purified by silica gel chromatography to give 455 mg (73% yield) of a mixture of (Z) and (E) esters in a 3.5:1 ratio. The mixture of esters (455 mg, 1.28 mmol) was dissolved in anhydrous dichloromethane (5.0 mL) and cooled to -78.degree. C. DIBAL in dichloromethane (3.2 mL of 1.0M solution, 3.2 mM) was added and the mixture stirred for 15 min. The reaction was quenched at -78.degree. C. using a saturated solution of Rochelle salt and extracted with dichloromethane. The organic layer was dried over MgSO.sub.4, then evaporated to give a white residue which was purified by chromatography to afford the corresponding cis allylic alcohol (211 mg) and trans allylic alcohol (37 mg). The cis-alcohol 2-[(Z)-3,4,5,6,7,8-hexahydro-4,4,5,5,8,8-hexamethyl-2H-anthracene-1-ylidin e] ethanol: .sup.1 H NMR (400 MHz, CDCl.sub.3) .delta. 7.25 (s, 1H, Ar), 7.03 (s, 1H, Ar), 5.57 (t, J=4.5 Hz, 1H), 4.43 (t, J=4.5 Hz, 2H), 2.46 (m, 2H), 1.75 (m, 2H), 1.67 (s, 4H), 1.28 (s, 18H). The trans-alcohol 2-[(E)-3,4,5,6,7,8-hexahydro-4,4,5,5,8,8-hexamethyl-2H-anthracene-1-ylidin e] ethanol; .sup.1 H NMR (400 MHz, CDCl.sub.3) .delta. 7.56 (s, 1H, Ar), 7.02 (s, 1H, Ar), 6.15 (t, J=4.5 Hz, 1H), 4.39 (t, J=4.5 Hz, 2H), 2.46 (m, 2H), 1.75 (m, 2H), 1.68 (s, 4H), 1.27 (s, 18H).

Detailed Description Text - DETX:

In the co-transfection assay, a cloned cDNA for an IR (e.g., human RAR.alpha., RAR.beta., RXR.gamma.) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled

element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX:

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be conveniently measured, e.g., by increasing **luciferase** production, which reflects compound-dependent, IR-mediated increases in reporter transcription. To detect antagonists, the co-transfection assay is carried out in the presence of a constant concentration of an agonist to the target IR (e.g., all-trans retinoic acid for RAR.alpha.) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., **luciferase** production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The basal reporter plasmid D-MTV-LUC (Hollenberg and Evans, 55 Cell, 899 (1988), the disclosure of which is herein incorporated by reference) containing two copies of the TRE-palindromic response element described in Umesono et al., 336 Nature, 262 (1988), the disclosure of which is herein incorporated by reference, was used in transfections for the RARs, and the reporter plasmid CRBPIIFKLUC, which contains an RXRE (retinoid X receptor response element, as described in Mangelsdorf et al., 66 Cell, 555 (1991), the disclosure of which is herein incorporated by reference), was used in transfections for the RXRs. Each of these reporter plasmids contains the cDNA for firefly **luciferase** (LUC) under constitutive promoter containing the appropriate RAR or RXR response element. As noted above, pRS-.beta.-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 5770382

DOCUMENT-IDENTIFIER: US 5770382 A

TITLE: Tricyclic retinoids, methods for their production and use

DATE-ISSUED: June 23, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hwang; Chan Kou	Boulder	CO	N/A	N/A
White; Steven K.	San Diego	CA	N/A	N/A
Badea; Beth Ann	San Diego	CA	N/A	N/A
Nadzan; Alex M.	San Diego	CA	N/A	N/A

APPL-NO: 08/ 475514

DATE FILED: June 7, 1995

PARENT-CASE:

REFERENCE TO RELATED APPLICATIONS This application is a Continuation-In-Part application of U.S. Pat. application Ser. No. 08/366,630, filed Dec. 30, 1994, now abandoned, the entire disclosure of which is herein incorporated by reference.

US-CL-CURRENT: 435/7.1; 514/217 ; 514/290 ; 514/454 ; 514/510 ; 514/569 ; 530/350 ; 530/369 ; 530/412 ; 540/586 ; 546/101 ; 549/388 ; 560/8 ; 562/405

ABSTRACT:

Tricyclic retinoids having activity for retinoic acid receptors and/or retinoid X receptors are provided. Also provided are pharmaceutical compositions incorporating such tricyclic retinoid compounds and methods for their therapeutic use.

39 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Brief Summary Text - BSTX:

These and various other advantages and features of **novelty** which characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the

be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX

A 50 mL round-bottom flask was flame-dried and charged with anhydrous THF (10 mL) and ethyl magnesium bromide (2.65 mL of 1M solution in THF, 2.65 mM) and the structure was cooled to 0.degree. C. Under a nitrogen atmosphere, a solution of ethyl ethynyl ether (0.375 mL of a 50% solution in hexanes, Aldrich Inc., 2.63 mM) was slowly added. The crude mixture was warmed to room temperature and stirred for 20 min. A solution of 4,4,5,5,8,8-hexamethyl-1,2,3,4,5,6,7,8-octahydroanthracen-1-one (0.50 g, 1.76 mmol) in THF (10 mL) was slowly added and stirring was continued for 2 h. The reaction mixture was quenched with a sat. solution of ammonium chloride and extracted with diethyl ether. The organic layer was dried over MgSO.sub.4, and the solvent evaporated. The crude residue was dissolved in ethanol (20 mL) and CO.sub.2 (dry ice) was **bubbled** through the solution for 3 h. After stirring for 12 h at 25.degree. C., the solvent was evaporated and the residue was purified by silica gel chromatography to give 455 mg (73% yield) of a mixture of (Z) and (E) esters in a 3.5:1 ratio. The mixture of esters (455 mg, 1.28 mmol) was dissolved in anhydrous dichloromethane (5.0 mL) and cooled to -78.degree. C. DIBAL in dichloromethane (3.2 mL of 1.0M solution, 3.2 mM) was added and the mixture stirred for 15 min. The reaction was quenched at -78.degree. C. using a saturated solution of Rochelle salt and extracted with dichloromethane. The organic layer was dried over MgSO.sub.4, then evaporated to give a white residue which was purified by chromatography to afford the corresponding cis allylic alcohol (211 mg) and trans allylic alcohol (37 mg). The cis-alcohol 2-[(Z)-3,4,5,6,7,8-hexahydro-4,4,5,5,8,8-hexamethyl-2H-anthracene-1-ylidin e] ethanol: .sup.1 H NMR (400 MHz, CDCl.sub.3) .delta. 7.25 (s, 1H, Ar), 7.03 (s, 1H, Ar), 5.57 (t, J=4.5 Hz, 1H), 4.43 (t, J=4.5 Hz, 2H), 2.46 (m, 2H), 1.75 (m, 2H), 1.67 (s, 4H), 1.28 (s, 18H). The trans-alcohol 2-[(E)-3,4,5,6,7,8-hexahydro-4,4,5,5,8,8-hexamethyl-2H-anthracene-1-ylidin e] ethanol; .sup.1 H NMR (400 MHz, CDCl.sub.3) .delta. 7.56 (s, 1H, Ar), 7.02 (s, 1H, Ar), 6.15 (t, J=4.5 Hz, 1H), 4.39 (t, J=4.5 Hz, 2H), 2.46 (m, 2H), 1.75 (m, 2H), 1.68 (s, 4H), 1.27 (s, 18H).

Detailed Description Text - DETX

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US-PAT-NO: 5770378

DOCUMENT-IDENTIFIER: US 5770378 A

TITLE: Tricyclic retinoids, methods for their production and use

DATE-ISSUED: June 23, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hwang; Chan Kou	Boulder	CO	N/A	N/A
White; Steven K.	San Diego	CA	N/A	N/A
Bennani; Youssef L.	La Jolla	CA	N/A	N/A
Canan Koch; Stacie S.	San Diego	CA	N/A	N/A
Badea; Beth Ann	San Diego	CA	N/A	N/A
Hebert; Jonathan J.	Mission Viejo	CA	N/A	N/A
Nadzan; Alex M.	San Diego	CA	N/A	N/A

APPL-NO: 08/ 472127

DATE FILED: June 7, 1995

PARENT-CASE:

REFERENCE TO RELATED APPLICATIONS This Application is a Continuation-In-Part application of U.S. Pat. application Ser. No. 08/366,630, filed Nov. 30, 1994, now abandoned, the entire disclosure of which is herein incorporated by reference.

US-CL-CURRENT: 435/7.1; 514/217 ; 514/290 ; 514/454 ; 514/510 ; 514/569 ; 530/350 ; 530/369 ; 530/412 ; 540/586 ; 546/101 ; 549/388 ; 560/8 ; 562/405

ABSTRACT:

Tricyclic retinoids having activity for retinoic acid receptors and/or retinoid X receptors are provided. Also provided are pharmaceutical compositions incorporating such tricyclic retinoid compounds and methods for their therapeutic use.

39 Claims, 0 Drawing figures

Exemplary Claim Number: 1

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Brief Summary Text - BSTX:

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Detailed Description Text - DETX:

In the co-transfection assay, a cloned cDNA for an IR (e.g., human RAR.alpha., RAR.beta., RXR.gamma.) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response

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Detailed Description Text - DETX:

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Detailed Description Text - DETX:

The basal reporter plasmid D-MTV-LUC (Hollenberg and Evans, 55 Cell, 899 (1988), the disclosure of which is herein incorporated by reference) containing two copies of the TRE-palindromic response element described in Umesono et al., 336 Nature, 262 (1988), the disclosure of which is herein incorporated by reference, was used in transfections for the RARs, and the reporter plasmid CRBPIIFKLUC, which contains an RXRE (retinoid X receptor response element, as described in Mangelsdorf et al., 66 Cell, 555 (1991), the disclosure of which is herein incorporated by reference), was used in transfections for the RXRs. Each of these reporter plasmids contains the cDNA for firefly **luciferase** (LUC) under constitutive promoter containing the appropriate RAR or RXR response element. As noted above, pRS-.beta.-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 5702887

DOCUMENT-IDENTIFIER: US 5702887 A

TITLE: Long emission wavelength chemiluminescent compounds and their use in test assays

DATE-ISSUED: December 30, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Law; Say-Jong	Westwood	MA	N/A	N/A
Jiang; Qingping	Norwood	MA	N/A	N/A
Fischer; Walter	Reinach	N/A	N/A	CH
Unger; John T.	Medfield	MA	N/A	N/A
Krodel; Elizabeth K.	Arlington	MA	N/A	N/A

APPL-NO: 08/ 340093

DATE FILED: November 14, 1994

PARENT-CASE:

This is a divisional of application Ser. No. 08/035,130 filed on Mar. 19, 1993, U.S. Pat. No. 5,395,752.

US-CL-CURRENT: 435/6; 252/700 ; 435/7.1 ; 436/501 ; 546/71

ABSTRACT:

An assay method incorporating at least two different chemiluminescent compounds for detection and/or quantitation of at least two substances in a test sample is described. The synthesis of chemiluminescent reagents or conjugates for use in such methods as well as kits incorporating such reagents are also disclosed. The assays have particular application in the field of clinical diagnostics.

21 Claims, 42 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 31

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Detailed Description Text - DETX:

(620 mg, 9.55 mmol) and copper(I) cyanide (391 mg, 4.43 mmol) in anhydrous methanol (16 ml) was **bubbled** with nitrogen for 1 minute and then kept in a sealed tube. The mixture was heated at 160.degree. C. with stirring for 4.5 hours and cooled. The red-brown mixture was evaporated and the residue was flash-chromatographed (W. C. still et al: J. Org. Chem., 43, 2923, (1978)) on a silica column (Baker silica gel, Cat #7024-1) packed with hexane and eluted with 10% ethyl acetate-hexane, yielding red 12-cyano-benz[b]acridine (1.54 g, 70%). Rf 0.7 (silica gel, hexane/ethyl acetate 2:1). MS (FAB, Thioglycerol Matrix): m/z 255 (M+1).

Detailed Description Text - DETX:

It is to be understood that various other modifications will be apparent to and can readily be made by those skilled in the art, given the disclosure herein, without departing from the Scope and materials of this invention. It is not, however, intended that the scope of the claims appended hereto be limited to the description as set forth herein, but rather that the claims be construed as encompassing all features of patentable **novelty** which reside in the present invention, including all features which would be treated as equivalents thereof by those skilled in the art to which the invention pertains. It is also noted that the examples given therein are intended to illustrate, and not to limit the invention.

Other Reference Publication - OREF:

Kinkel, et al., "Synthesis and Properties of New Luminescent Acridinium-9-carboxylic Acid Derivatives and their Application in Luminescence Immunoassays (LIA)", Journal of **Bioluminescence** and Chemiluminescence, 4:136-139, 1989.

Other Reference Publication - OREF:

Mattingly, P., "Chemiluminescent 10-Methyl-Acridinium-9-(N-Sulphonylcarboxamide) Salts. Synthesis and Kinetics of Light Emission", Journal of **Bioluminescence** and Chemiluminescence, 6:107-114, 1991.

US-PAT-NO: 5696133

DOCUMENT-IDENTIFIER: US 5696133 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: December 9, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jones; Todd K.	Solana Beach	CA	N/A	N/A
Goldman; Mark E.	San Diego	CA	N/A	N/A
Pooley; Charlotte L.F.	San Diego	CA	N/A	N/A
Winn; David T.	San Diego	CA	N/A	N/A
Edwards; James P.	San Diego	CA	N/A	N/A
West; Sarah J.	San Diego	CA	N/A	N/A
Tegley; Christopher M.	San Diego	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A
Hamann; Lawrence G.	San Diego	CA	N/A	N/A
Farmer; Luc J.	La Jolla	CA	N/A	N/A
Davis; Robert L.	Santee	CA	N/A	N/A

APPL-NO: 08/ 465556

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 23, 1994 abandoned, the entire disclosure of which is herein incorporated by reference.

US-CL-CURRENT: 514/314; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/252.04 ; 514/253.06 ; 514/253.07 ; 514/256 ; 514/267 ; 514/291 ; 514/292 ; 514/311 ; 514/312

ABSTRACT:

Non-steroidal compounds which are high affinity, high selectivity modulators for steroid receptors are disclosed. Also disclosed are pharmaceutical compositions incorporating such compounds, methods for employing the disclosed compounds and compositions for treating patients requiting steroid receptor agonist or antagonist therapy, intermediates useful in the preparation of the compounds and processes for the preparation of the steroid receptor modulator compounds.

10 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Brief Summary Text - BSTX:

These and various other advantages and features of **novelty** which characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX:

6-(5-Fluoro-3-nitrophenyl)-1,2-dihydro-2,2,4-trimethylquinoline (Compound 280, structure 4 of Scheme II, where R.sup.1 =5-fluoro-3-nitrophenyl) 1-Fluoro-3-nitroiodobenzene To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg, 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was **bubbled** through the colorless solution for 15 min. The solution was cooled to 0.degree. C. in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was placed in an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50%) of 5-fluoro-3-nitroiodobenzene. Data for 5-fluoro-3-nitroiodobenzene: .sup.1 H NMR (400 MHz, acetone-d.sub.6) 8.36 (s, 1 H), 8.00 (m, 2 H).

Detailed Description Text - DETX:

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX:

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be conveniently measured, e.g., by increasing **luciferase** production, which reflects compound-dependent, IR-mediated increases in reporter transcription. To detect antagonists, the co-transfection assay is carried out in the presence of a constant concentration of an agonist to the target IR (e.g., progesterone for PR) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., **luciferase** production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing a progesterone response element. This plasmid is more fully described in Berger et al. supra. In addition, for ER agonist and antagonist determinations, the reporter plasmid MTV-ERE5-LUC, which contains LUC under control of the mouse mammary tumor virus (MTV) long terminal repeat in which the glucocorticoid response elements have been deleted and replaced with five copies of a 33-base pair ERE as described in Tzukerman et al., supra, was substituted for the MTV-LUC plasmid described herein. pRS-.beta.-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 5696130

DOCUMENT-IDENTIFIER: US 5696130 A

TITLE: Tricyclic steroid receptor modulator compounds and methods

DATE-ISSUED: December 9, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jones; Todd K.	Solana Beach	CA	N/A	N/A
Winn; David T.	San Diego	CA	N/A	N/A
Goldman; Mark E.	San Diego	CA	N/A	N/A
Hamann; Lawrence G.	San Diego	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A
Farmer; Luc J.	La Jolla	CA	N/A	N/A
Davis; Robert L.	Santee	CA	N/A	N/A

APPL-NO: 08/ 462643

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of United States patent application Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned, the entire disclosure of which is herein incorporated by reference.

US-CL-CURRENT: 514/291; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/252.04 ; 514/253.03 ; 514/255.05 ; 514/256 ; 514/292 ; 514/411 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/338 ; 544/342 ; 544/343 ; 544/344 ; 544/353 ; 546/81 ; 546/84 ; 546/89 ; 546/92 ; 548/432

ABSTRACT:

Non-steroidal compounds which are high affinity, high selectivity modulators for steroid receptors are disclosed. Also disclosed are pharmaceutical compositions incorporating such compounds, methods for employing the disclosed compounds and compositions for treating patients requiring steroid receptor agonist or antagonist therapy, intermediates useful in the preparation of the compounds and processes for the preparation of the steroid receptor modulator compounds.

35 Claims, 0 Drawing figures

Exemplary Claim Number: 1

Brief Summary Text - BSTX:

These and various other advantages and features of **novelty** which characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX

1-Fluoro-3-nitroiodobenzene To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg, 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was **bubbled** through the colorless solution for 15 min. The solution was cooled to 0.degree. C. in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was placed in an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50%) of 5-fluoro-3-nitroiodobenzene. Data for 5-fluoro-3-nitroiodobenzene: sup.1 H NMR (400 MHz, acetone-d6) 8.36 (s, 1 H), 8.00 (m, 2 H).

Detailed Description Text - DETX

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX.

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be

reflects compound-dependent, IR-mediated increases in reporter transcription. To detect antagonists, the co-transfection assay is carried out in the presence of a constant concentration of an agonist to the target IR (e.g., progesterone for PR) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., **luciferase** production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing a progesterone response element. This plasmid is more fully described in Berger et al. supra. In addition, for ER agonist and antagonist determinations, the reporter plasmid MTV-ERE5-LUC, which contains LUC under control of the mouse mammary tumor virus (MTV) long terminal repeat in which the glucocorticoid response elements have been deleted and replaced with five copies of a 33-base pair ERE as described in Tzukerman et al., supra, was substituted for the MTV-LUC plasmid described herein. pRS-B-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 5696127

DOCUMENT-IDENTIFIER: US 5696127 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: December 9, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jones; Todd K.	Solana Beach	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A
Edwards; James P.	San Diego	CA	N/A	N/A
Tegley; Christopher M.	San Diego	CA	N/A	N/A
West; Sarah J.	San Diego	CA	N/A	N/A

APPL-NO: 08/ 465429

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned the entire disclosure of which is herein incorporated by reference.

US-CL-CURRENT: 514/285; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/252.04 ; 514/253.02 ; 514/255.05 ; 514/256 ; 514/267 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/338 ; 544/342 ; 544/344 ; 544/353 ; 546/62

ABSTRACT:

Non-steroidal compounds which are high affinity, high selectivity modulators for steroid receptors are disclosed. Also disclosed are pharmaceutical compositions incorporating such compounds, methods for employing the disclosed compounds and compositions for treating patients requiring steroid receptor agonist or antagonist therapy, intermediates useful in the preparation of the compounds and processes for the preparation of the steroid receptor modulator compounds.

36 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Brief Summary Text (BSTX)

These and various other advantages and features of **novelty** which characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX:

To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg, 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was **bubbled** through the colorless solution for 15 min. The solution was cooled to 0.degree. C. in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was placed in an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50%) of 5-fluoro-3-nitroiodobenzene. Data for 5-fluoro-3-nitroiodobenzene: .sup.1 H NMR (400 MHz, acetone-d6) 8.36 (s, 1H), 8.00 (m, 2H).

Detailed Description Text - DETX:

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX:

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be conveniently measured, e.g., by increasing **luciferase** production, which reflects compound-dependent, IR-mediated increases in reporter transcription. To detect antagonists, the co-transfection assay is carried out in the presence

for PR) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., **luciferase** production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing a progesterone response element. This plasmid is more fully described in Berger et al. supra. In addition, for ER agonist and antagonist determinations, the reporter plasmid MTV-ERE5-LUC, which contains LUC under control of the mouse mammary tumor virus (MTV) long terminal repeat in which the glucocorticoid response elements have been deleted and replaced with five copies of a 33-base pair ERE as described in Tzukerman et al., supra, was substituted for the MTV-LUC plasmid described herein. pRS-.beta.-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 5693647

DOCUMENT-IDENTIFIER: US 5693647 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: December 2, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jones; Todd K.	Solana Beach	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A
Tegley; Christopher M.	San Diego	CA	N/A	N/A
Winn; David T.	San Diego	CA	N/A	N/A
Hamann; Lawrence G.	San Diego	CA	N/A	N/A
Edwards; James P.	San Diego	CA	N/A	N/A
West; Sarah J.	San Diego	CA	N/A	N/A

APPL-NO: 08/ 464546

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994 now abandoned, the entire disclosure of which is herein incorporated by reference.

US-CL-CURRENT: 514/285; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/255.05 ; 514/256 ; 514/267 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/333 ; 544/342 ; 544/343 ; 544/344 ; 544/353 ; 546/62 ; 546/70 ; 546/77 ; 546/78

ABSTRACT:

Non-steroidal compounds which are high affinity, high selectivity modulators for steroid receptors are disclosed. Also disclosed are pharmaceutical compositions incorporating such compounds, methods for employing the disclosed compounds and compositions for treating patients requiring steroid receptor agonist or antagonist therapy, intermediates useful in the preparation of the compounds and processes for the preparation of the steroid receptor modulator compounds.

27 Claims, 0 Drawing figures

Exemplary Claim Number: 1

Brief Summary Text - BSTX:

These and various other advantages and features of **novelty** which characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX:

To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg, 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was **bubbled** through the colorless solution for 15 min. The solution was cooled to 0.degree. C. in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was placed in an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50%) of 5-fluoro-3-nitroiodobenzene. Data for 5-fluoro-3-nitroiodobenzene: .sup.1 H NMR (400 MHz, acetone-d.sub.6) 8.36 (s, 1H), 8.00 (m, 2H).

Detailed Description Text - DETX:

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX:

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be

reflects compound-dependent, IR-mediated increases in reporter transcription. To detect antagonists, the co-transfection assay is carried out in the presence of a constant concentration of an agonist to the target IR (e.g., progesterone for PR) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., **luciferase** production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing a progesterone response element. This plasmid is more fully described in Berger et al. supra. In addition, for ER agonist and antagonist determinations, the reporter plasmid MTV-ERE5-LUC, which contains LUC under control of the mouse mammary tumor virus (MTV) long terminal repeat in which the glucocorticoid response elements have been deleted and replaced with five copies of a 33-base pair ERE as described in Tzukerman et al., supra, was substituted for the MTV-LUC plasmid described herein. pRS-.beta.-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 5693646

DOCUMENT-IDENTIFIER: US 5693646 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: December 2, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jones; Todd K.	Solana Beach	CA	N/A	N/A
Tegley; Christopher M.	San Diego	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A
Edwards; James P.	San Diego	CA	N/A	N/A
West; Sarah J.	San Diego	CA	N/A	N/A

APPL-NO: 08/ 464360

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994 abandoned, the entire disclosure of which is herein incorporated by reference.

US-CL-CURRENT: 514/285; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/253.02 ; 514/256 ; 514/267 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/338 ; 544/342 ; 544/343 ; 544/344 ; 544/353 ; 546/62

ABSTRACT:

Non-steroidal compounds which are high affinity, high selectivity modulators for steroid receptors are disclosed. Also disclosed are pharmaceutical compositions incorporating such compounds, methods for employing the disclosed compounds and compositions for treating patients requiring steroid receptor agonist or antagonist therapy, intermediates useful in the preparation of the compounds and processes for the preparation of the steroid receptor modulator compounds.

28 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

These and various other advantages and features of **novelty** which characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX:

To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg, 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was **bubbled** through the colorless solution for 15 min. The solution was cooled to 0.degree. C. in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was placed in an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50%) of 5-fluoro-3-nitroiodobenzene. Data for 5-fluoro-3-nitroiodobenzene: .sup.1 H NMR (400 MHz, acetone-d.sub.6) 8.36 (s, 1 H), 8.00 (m, 2 H).

Detailed Description Text - DETX:

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX:

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be conveniently measured, e.g., by increasing **luciferase** production, which reflects compound-dependent, IR-mediated increases in reporter transcription. To detect antagonists, the co-transfection assay is carried out in the presence

for PR) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., **luciferase** production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing a progesterone response element. This plasmid is more fully described in Berger et al. supra. In addition, for ER agonist and antagonist determinations, the reporter plasmid MTV-ERE5-LUC, which contains LUC under control of the mouse mammary tumor virus (MTV) long terminal repeat in which the glucocorticoid response elements have been deleted and replaced with five copies of a 33-base pair ERE as described in Tzukerman et al., supra, was substituted for the MTV-LUC plasmid described herein. pRS-.beta.-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 5688810

DOCUMENT-IDENTIFIER: US 5688810 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: November 18, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jones; Todd K.	Solana Beach	CA	N/A	N/A
Goldman; Mark E.	San Diego	CA	N/A	N/A
Pooley; Charlotte L.F.	San Diego	CA	N/A	N/A
Winn; David T.	San Diego	CA	N/A	N/A
Edwards; James P.	San Diego	CA	N/A	N/A
West; Sarah J.	San Diego	CA	N/A	N/A
Tegley; Christopher M.	San Diego	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A

APPL-NO: 08/ 464541

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned, the entire disclosure of which is herein incorporated by reference.

US-CL-CURRENT: 514/311; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/252.04 ; 514/255.05 ; 514/256 ; 514/267 ; 514/314 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/333 ; 544/338 ; 544/342 ; 544/353 ; 546/152 ; 546/167 ; 546/168 ; 546/173 ; 546/178 ; 546/180

ABSTRACT:

Non-steroidal compounds which are high affinity, high selectivity modulators for steroid receptors are disclosed. Also disclosed are pharmaceutical compositions incorporating such compounds, methods for employing the disclosed compounds and compositions for treating patients requiring steroid receptor agonist or antagonist therapy, intermediates useful in the preparation of the compounds and processes for the preparation of the steroid receptor modulator compounds.

27 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Brief Summary Text - BSTX:

These and various other advantages and features of **novelty** which characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX:

To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg, 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was **bubbled** through the colorless solution for 15 min. The solution was cooled to 0.degree. C. in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was placed in an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50%) of 5-fluoro-3-nitroiodobenzene. Data for 5-fluoro-3-nitroiodobenzene: .sup.1 H NMR (400 MHz, acetone-d.sub.6) 8.36 (s, 1H), 8.00 (m, 2H).

Detailed Description Text - DETX:

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX:

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound

conveniently measured, e.g., by increasing **luciferase** production, which reflects compound-dependent, IR-mediated increases in reporter transcription. To detect antagonists, the co-transfection assay is carried out in the presence of a constant concentration of an agonist to the target IR (e.g., progesterone for PR) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., **luciferase** production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing a progesterone response element. This plasmid is more fully described in Berger et al. supra. In addition, for ER agonist and antagonist determinations, the reporter plasmid MTV-ERE5-LUC, which contains LUC under control of the mouse mammary tumor virus (MTV) long terminal repeat in which the glucocorticoid response elements have been deleted and replaced with five copies of a 33-base pair ERE as described in Tzukerman et al., supra, was substituted for the MTV-LUC plasmid described herein. pRS-.beta.-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

US-PAT-NO: 5688808

DOCUMENT-IDENTIFIER: US 5688808 A

TITLE: Steroid receptor modulator compounds and methods

DATE-ISSUED: November 18, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Jones; Todd K.	Solana Beach	CA	N/A	N/A
Winn; David T.	San Diego	CA	N/A	N/A
Zhi; Lin	San Diego	CA	N/A	N/A
Hamann; Lawrence G.	San Diego	CA	N/A	N/A
Tegley; Christopher M.	San Diego	CA	N/A	N/A
Pooley; Charlotte L. F.	San Diego	CA	N/A	N/A

APPL-NO: 08/ 463231

DATE FILED: June 5, 1995

PARENT-CASE:

RELATED PATENT APPLICATIONS This application is a Continuation-In-Part of U.S. patent application Ser. No. 08/363,529, filed Dec. 22, 1994, abandoned the entire disclosure of which is herein incorporated by reference.

US-CL-CURRENT: 514/285; 514/242 ; 514/243 ; 514/246 ; 514/247 ; 514/248 ; 514/249 ; 514/250 ; 514/252.04 ; 514/255.05 ; 514/256 ; 514/267 ; 544/179 ; 544/180 ; 544/183 ; 544/233 ; 544/234 ; 544/235 ; 544/238 ; 544/245 ; 544/246 ; 544/249 ; 544/284 ; 544/333 ; 544/342 ; 544/343 ; 544/344 ; 544/353 ; 546/62 ; 546/70 ; 546/77 ; 546/78

ABSTRACT:

Non-steroidal compounds which are high affinity, high selectivity modulators for steroid receptors are disclosed. Also disclosed are pharmaceutical compositions incorporating such compounds, methods for employing the disclosed compounds and compositions for treating patients requiring steroid receptor agonist or antagonist therapy, intermediates useful in the preparation of the compounds and processes for the preparation of the steroid receptor modulator compounds.

27 Claims, 0 Drawing figures

Exemplary Claim Number: 1

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Brief Summary Text - BSTX:

These and various other advantages and features of **novelty** which characterize the invention are pointed out with particularity in the claims annexed hereto and forming a part hereof. However, for a better understanding of the invention, its advantages, and objects obtained by its use, reference should be had to the accompanying drawings and descriptive matter, in which there is illustrated and described preferred embodiments of the invention.

Detailed Description Text - DETX

To a 25 mL round-bottom flask equivuipped with a magnetic stir bar 3-iodo-5-nitroaniline (543.3 mg, 2.06 mmol) and methylene chloride (10 mL) were added under nitrogen. Nitrogen was **bubbled** through the colorless solution for 15 min. The solution was cooled to 0.degree. C. in an ice bath. At that point approximately 500 mg nitrosonium tetrafluoroborate was added in one portion making a cloudy precipitate. The reaction was allowed to continue stirring for 2 hours. The mixture was kept under nitrogen as 10 mL dry, deoxygenated ortho-dichlorobenzene was added. A distillation apparatus was fitted to the reaction flask. The flask was placed in an oil bath and was heated until the material had completely distilled over. The crude product was isolated by washing the residue through a short column (74 mL silica, hexane). Purification by silica gel chromatography (74 mL silica, hexane) afforded 279.4 mg (50%) of 5-fluoro-3-nitroiodobenzene. Data for 5-fluoro-3-nitroiodobenzene: .sup.1 H NMR (400 MHz, acetone-d.sub.6) 8.36 (s, 1H), 8.00 (m, 2H).

Detailed Description Text - DETX

In the co-transfection assay, a cloned cDNA for an IR (e.g., human PR, AR or GR) under the control of a constitutive promoter (e.g., the SV 40 promoter) is introduced by transfection (a procedure to induce cells to take up foreign genes) into a background cell substantially devoid of endogenous IRs. This introduced gene directs the recipient cells to make the IR protein of interest. A second gene is also introduced (co-transfected) into the same cells in conjunction with the IR gene. This second gene, comprising the cDNA for a reporter protein, such as firefly **luciferase** (LUC), controlled by an appropriate hormone responsive promoter containing a hormone response element (HRE). This reporter plasmid functions as a reporter for the transcription-modulating activity of the target IR. Thus, the reporter acts as a surrogate for the products (mRNA then protein) normally expressed by a gene under control of the target receptor and its native hormone.

Detailed Description Text - DETX

The co-transfection assay can detect small molecule agonists or antagonists of target IRs. Exposing the transfected cells to an agonist ligand compound increases reporter activity in the transfected cells. This activity can be conveniently measured, e.g., by increasing **luciferase** production, which

To detect antagonists, the co-transfection assay is carried out in the presence of a constant concentration of an agonist to the target IR (e.g., progesterone for PR) known to induce a defined reporter signal. Increasing concentrations of a suspected antagonist will decrease the reporter signal (e.g., **luciferase** production). The co-transfection assay is therefore useful to detect both agonists and antagonists of specific IRs. Furthermore, it determines not only whether a compound interacts with a particular IR, but whether this interaction mimics (agonizes) or blocks (antagonizes) the effects of the native regulatory molecules on target gene expression, as well as the specificity and strength of this interaction.

Detailed Description Text - DETX:

The reporter plasmid, MTV-LUC, contains the cDNA for firefly **luciferase** (LUC) under control of the mouse mammary tumor virus (MTV) long terminal repeat, a conditional promoter containing a progesterone response element. This plasmid is more fully described in Berger et al. supra. In addition, for ER agonist and antagonist determinations, the reporter plasmid MTV-ERE5-LUC, which contains LUC under control of the mouse mammary tumor virus (MTV) long terminal repeat in which the glucocorticoid response elements have been deleted and replaced with five copies of a 33-base pair ERE as described in Tzukerman et al., supra, was substituted for the MTV-LUC plasmid described herein. pRS-.beta.-Gal, coding for constitutive expression of E. coli .beta.-galactosidase (.beta.-Gal), was included as an internal control for evaluation of transfection efficiency and compound toxicity.

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DOCUMENT-IDENTIFIER: US 5521067 A

TITLE: Bone marrow cell adhesion molecules and process for detecting adherence between cell adhesion molecules and cells generally

DATE-ISSUED: May 28, 1996

INVENTOR-INFORMATION:

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APPL-NO: 08/ 158936

DATE FILED: November 24, 1993

US-CL-CURRENT: 435/7.24; 435/29 ; 435/7.2 ; 435/7.9 ; 435/961 ; 435/962 ; 436/516 ; 436/63

ABSTRACT:

The present invention relates to proteins associated with human bone marrow cell membranes for adhering hematopoietic cells to human bone marrow cell membranes. These proteins are soluble in lithium dodecyl sulfate but insoluble in 2% nonaethylene glycol octylphenol ether (e.g., 2% Triton.RTM. X-100) solution. These proteins and antibodies raised against them are useful in the treatment and diagnosis of blood disorders. The DNA molecules encoding these proteins have use in gene therapy regimes. Also disclosed is a method for detecting binding between cell adhesion membrane proteins and cells having a potential to be bound to such proteins.

8 Claims, 40 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 11

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Detailed Description Text - DETX:

The assay system may have a sandwich or competitive format. Examples of suitable assays include an enzyme-linked immunosorbent assay, a radioimmunoassay, a gel diffusion precipitant reaction assay, an immunodiffusion assay, an agglutination assay, a **fluorescent immunoassay, a protein** A immunoassay, an immunoblotting assay, an immunoperoxidase assay, an

assay.

Detailed Description Text - DETX:

Target cells were washed once in PBS-CMF by centrifugation, resuspended in 30 ml of 1% BSA/PBS(+), counted (.about.3.times.10.sup.6 /ml), and stored on ice until the blot was ready for cell incubation. Following overnight incubation of the blot, the blocking solution was removed and the blot was washed in cold 0.5% BSA/PBS(+) for 3.times.5 min with gentle rocking during the first two washes and with no rocking during the last wash. During the last wash and prior to the addition of cells, it was again checked to see that the membrane remained flat at the bottom of the vessel. The last wash solution was removed; the blot was centered in the vessel with a fine curved forceps; cell suspension was mixed with a 10 ml pipet and then slowly added to the center of the blot avoiding any air **bubbles**. The vessel was covered with a large plastic container and incubated in the cold room (4.degree. C.) for 90 min for the cells to settle on the blot and adhere to the specific protein bands. At the end of cell incubation, the vessel was brought out of the cold room, slightly lifted and tilted to a corner, and the cell suspension was aspirated from the corner using a 25 ml pipet. Then blots were washed 3.times.5 min using cold 0.5% BSA/PBS(+) at room temperature. To minimize turbulence, all washes were added using a 25 ml pipet (20 ml/wash) by placing the pipet tip to the side of the chamber and were aspirated from a corner by tilting of the vessel so that all fluid was removed. After aspirating each wash, the blot was gently pushed to one end of the chamber with a fine forceps and then fresh wash solution was added to the chamber away from the blot. This washing procedure was found to be optimal; and no rocking of the vessel was attempted during the procedure. Thus simply adding and removing the wash solution was adequate to remove all the nonadherent cells and provide a clean background.

Detailed Description Text - DETX:

Western blotting of stromal cell membrane protein extracts using monoclonal antibodies to VCAM-1, CD54 and CD44 have identified all three molecules in the Triton.RTM. X-100 extracts (FIGS. 12A, 12B, 12C) but not the LDS extract. This is consistent with the observation that these molecules can be immunoprecipitated from Triton.RTM. X-100 lysates of stromal cells (Simmons P. J., Masinovsky B., Longenecker B. M., Berenson R., Torok-Storb B., Gallatin W. M., Blood 80: 388 (1992), which is hereby incorporated by reference). The electrophoretic mobilities of the known CAMs are remarkably different from those of the BM CAMs reported here pointing to **novelty** of the BM CAMs.